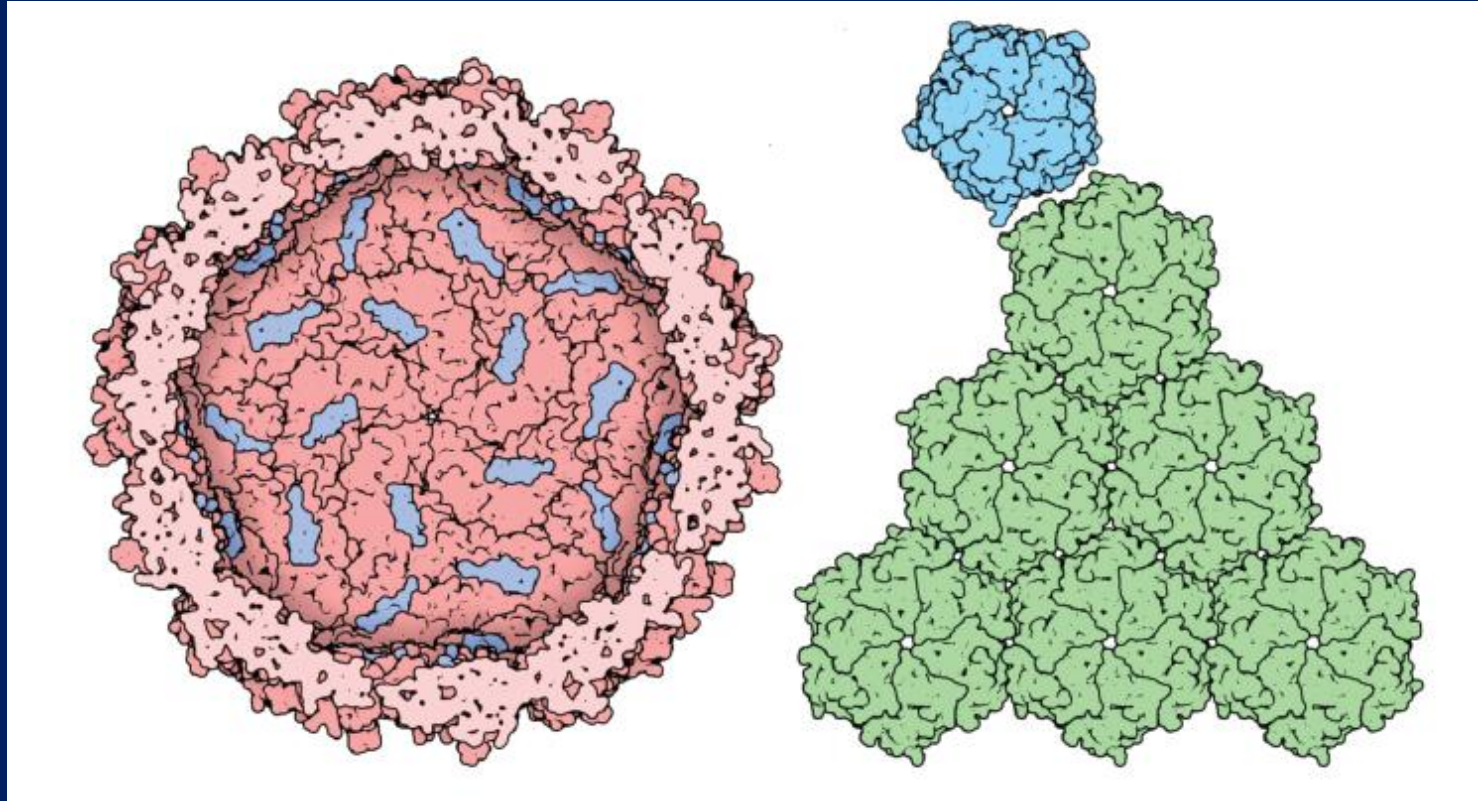


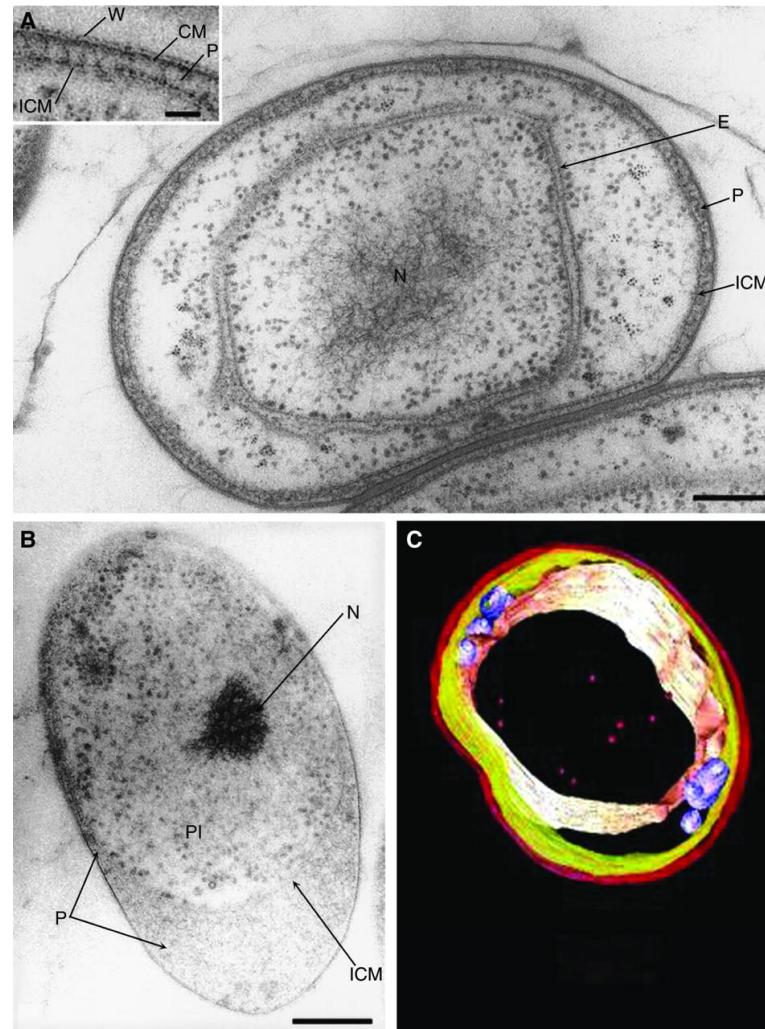
Integration of metabolism

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metabolic reactions are compartmented; biosynthesis and catabolism are usually separated in space

Bacterial microcompartments



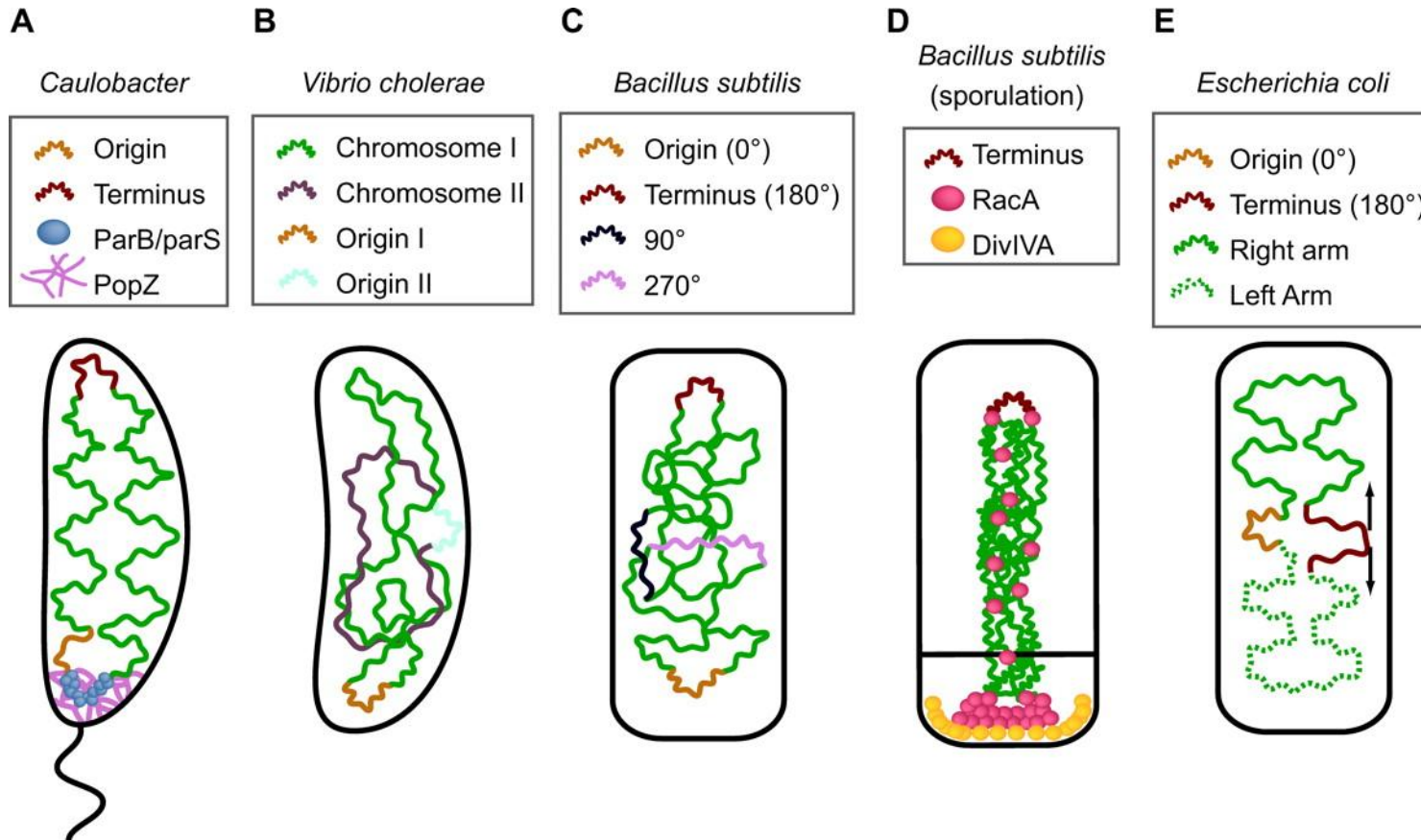
The nucleus-like organelle of *Gemmata obscuriglobus* is shown in (A).



Murat D et al. Cold Spring Harb Perspect Biol
2010;2:a000422

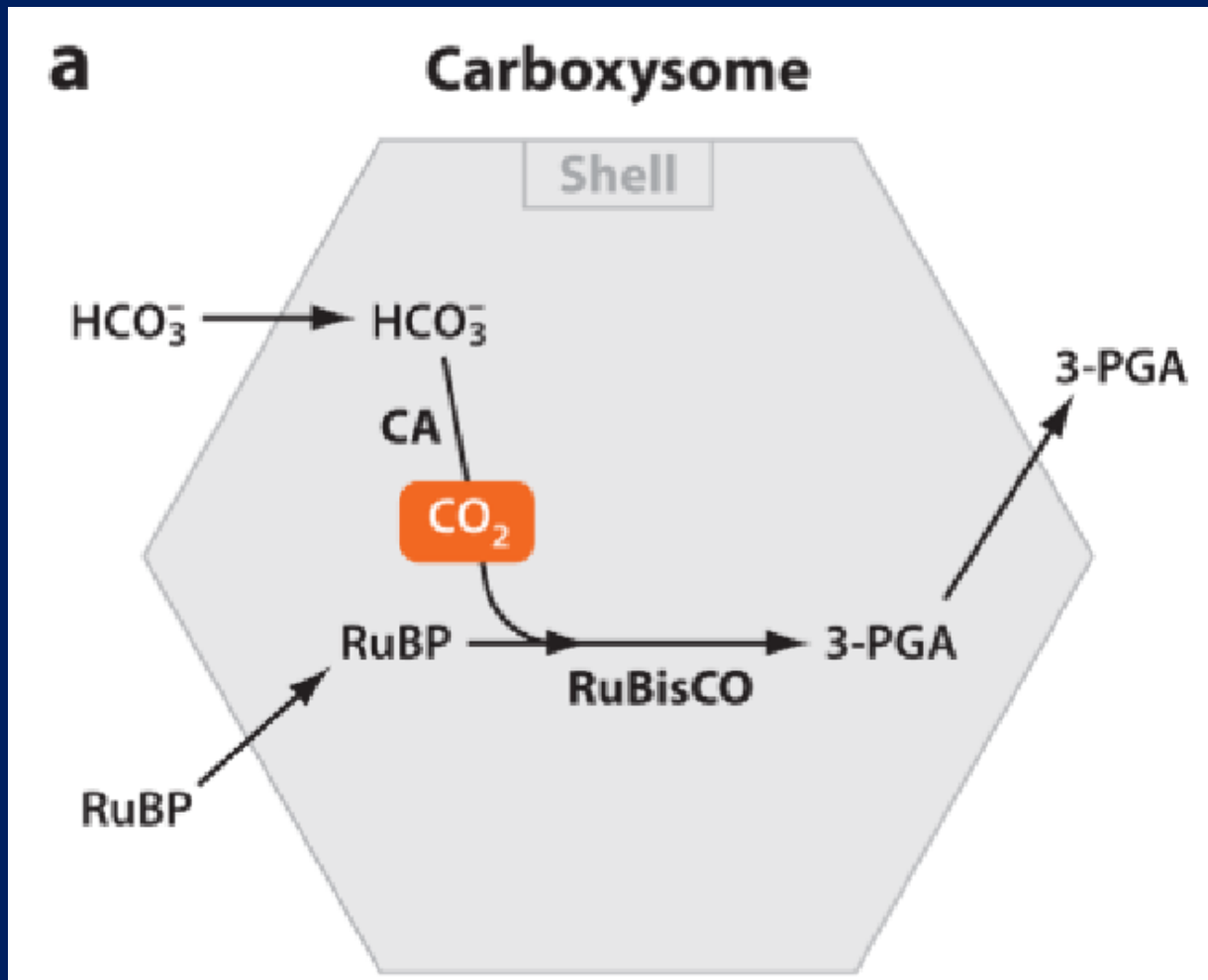


Chromosome organization in model bacteria.

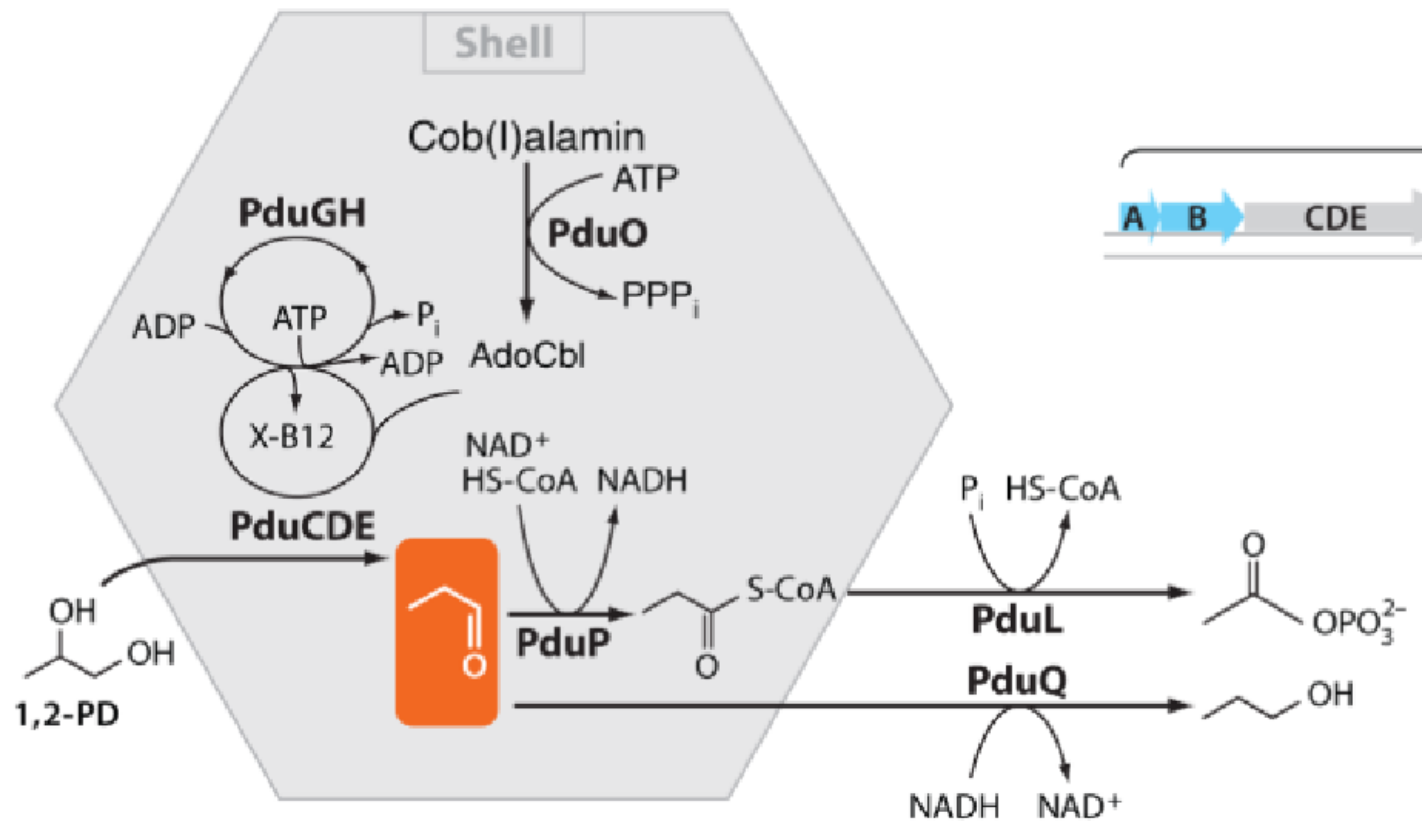


Toro E , and Shapiro L Cold Spring Harb Perspect Biol
2010;2:a000349

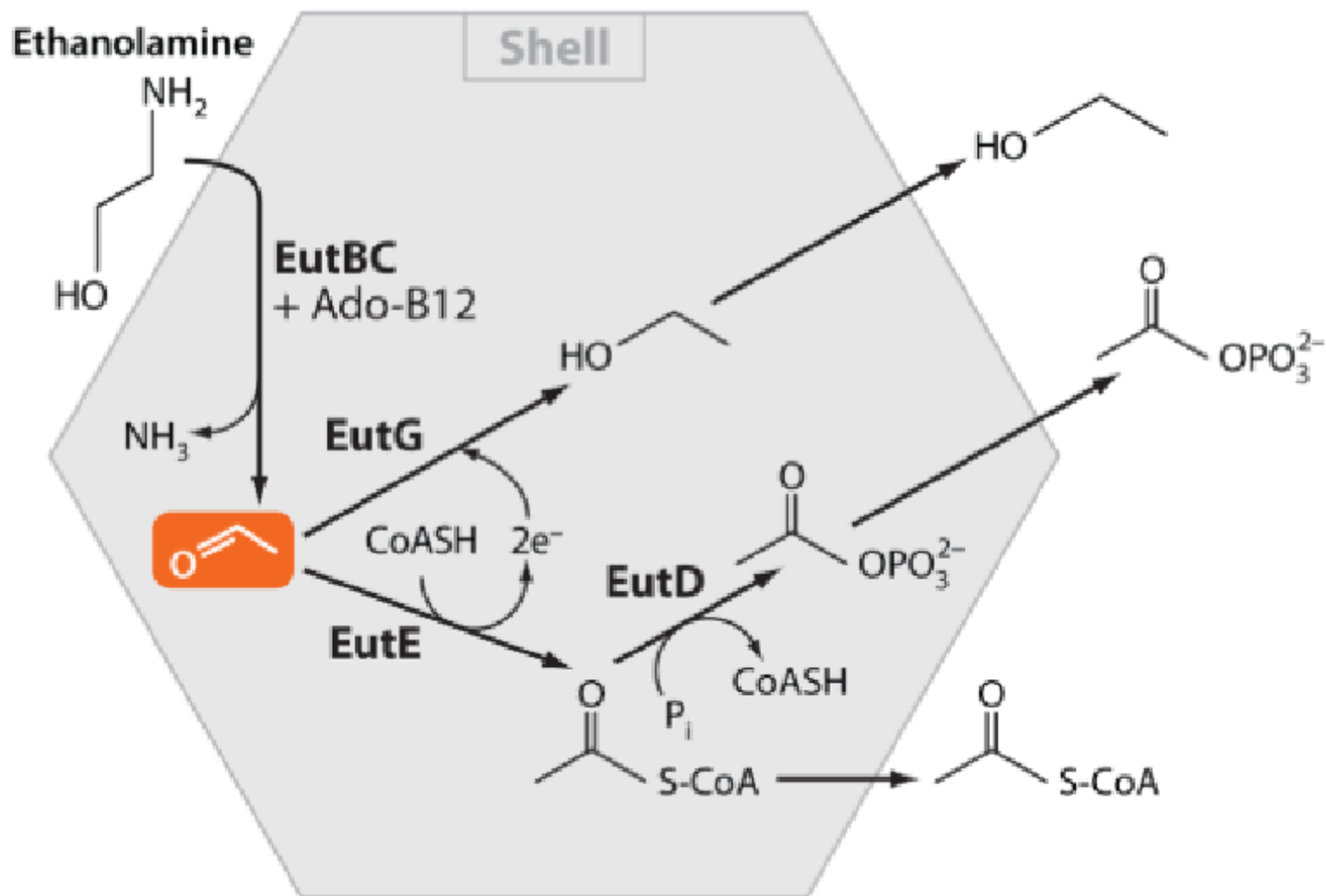
Metabolic specificity of microcompartments



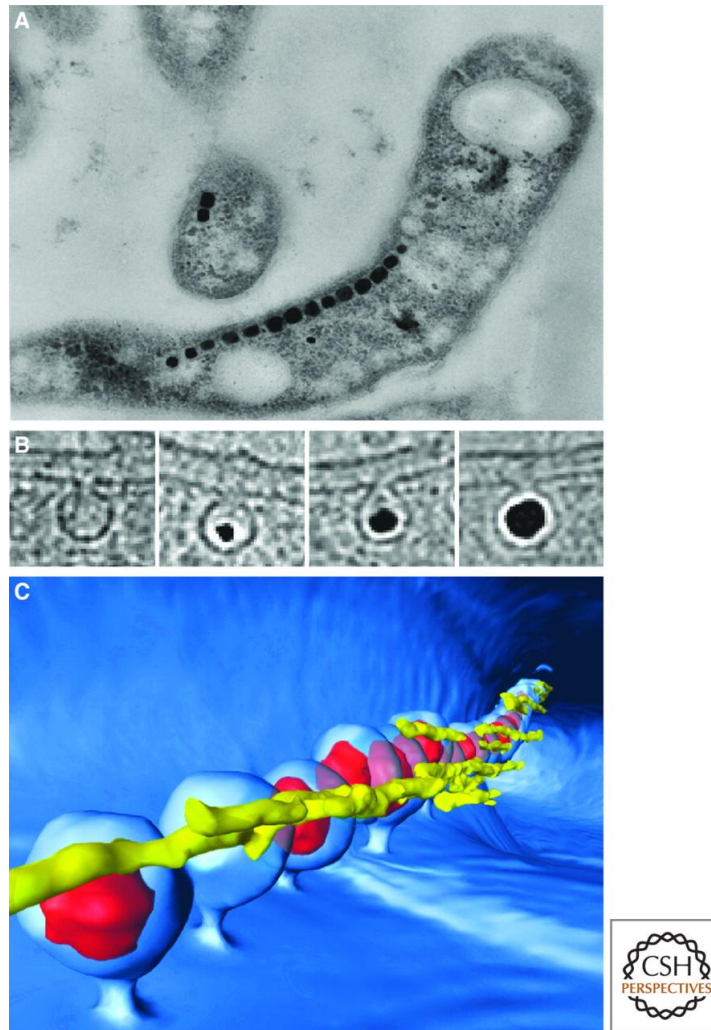
b Propanediol utilization (Pdu)



C Ethanolamine utilization (Eut)

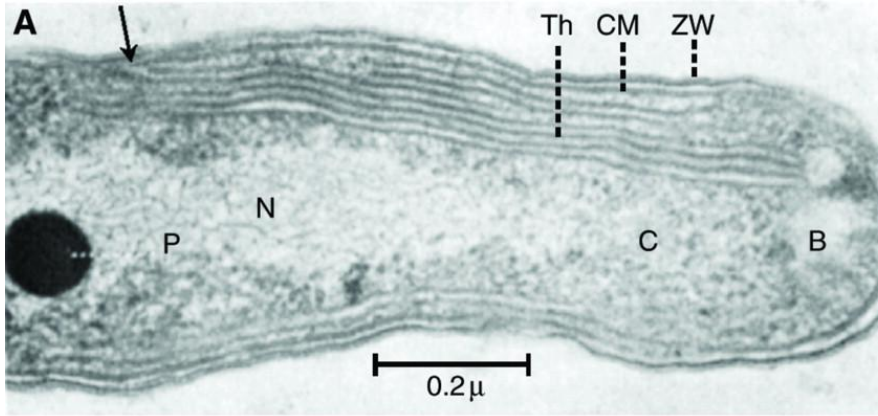


Magnetosomes can be easily visualized with various forms of electron microscopy.

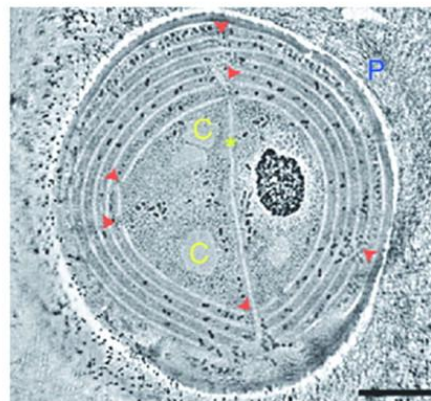
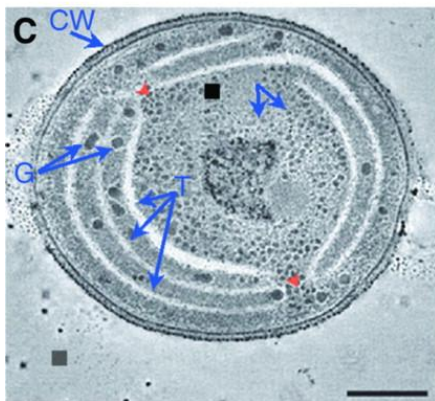
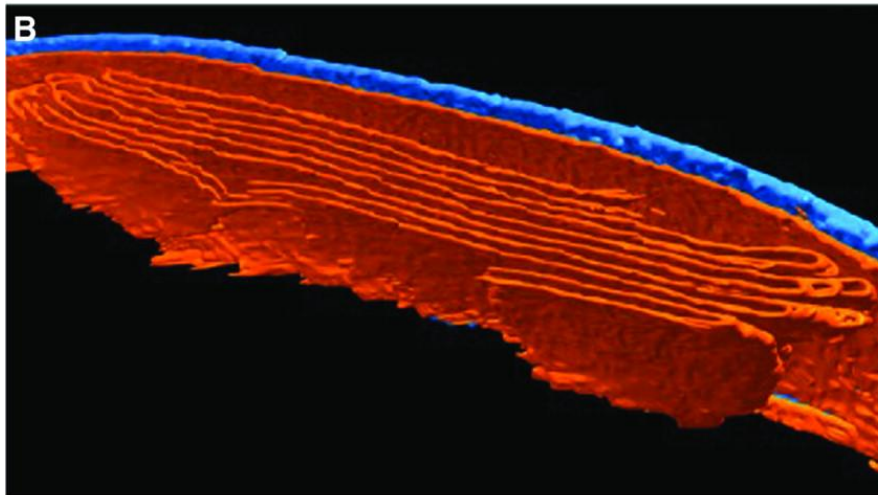


**Murat D et al. Cold Spring Harb Perspect Biol
2010;2:a000422**



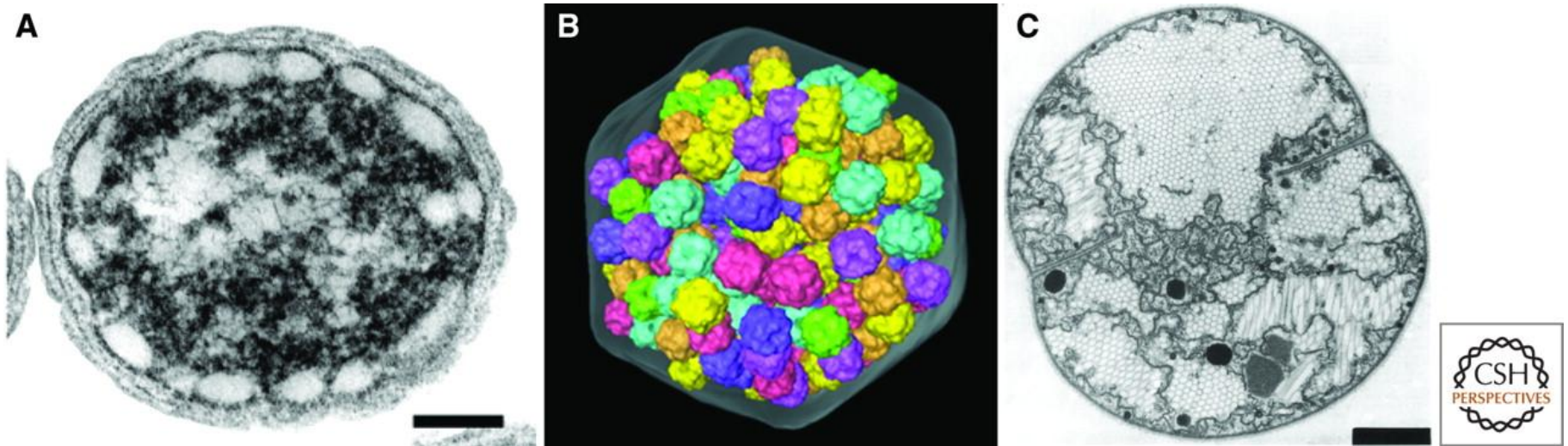


**Photosynthetic membranes
were the first of bacterial
organelles to be imaged with
electron microscopy.**



**Murat D et al. Cold Spring Harb Perspect
Biol 2010;2:a000422**

Chlorosomes of *Chlorobium tepidum* appear as flattened ovals arranged around the cell periphery (A).



**Murat D et al. Cold Spring Harb Perspect Biol
2010;2:a000422**

Hierarchical assembly of typical bacterial microcompartment

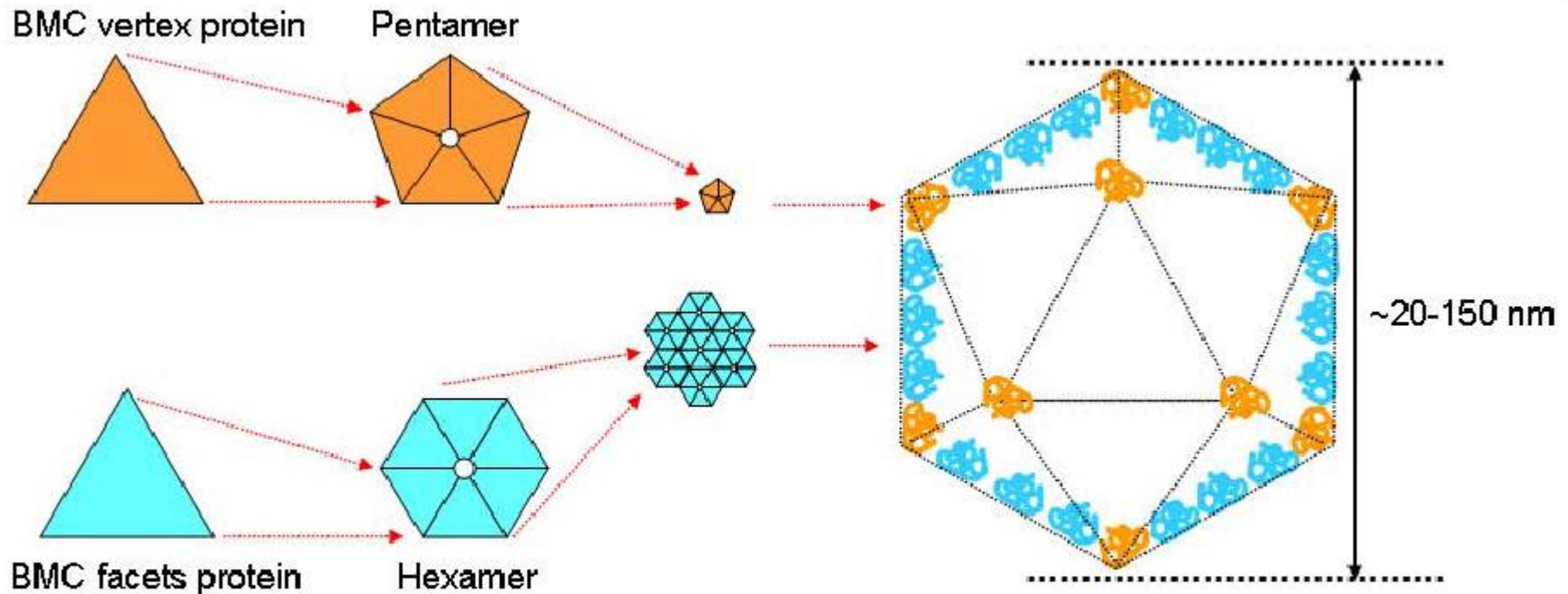
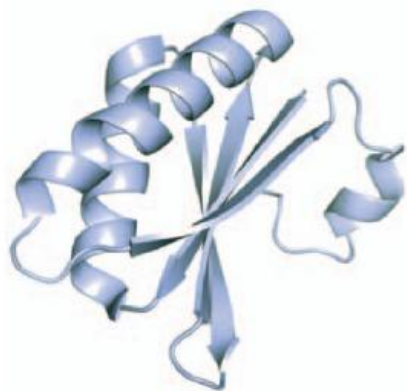
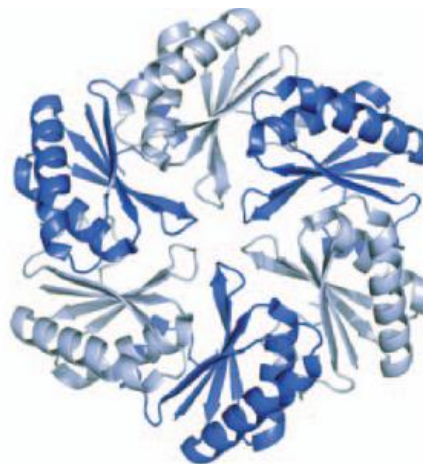


Figure 1 Model for the hierarchical assembly of a typical bacterial microcompartment. The facets of these icosahedral nano-cages are made of one type of protein (in light blue) that further self-assemble to give hexamers. On the other hand, the vertices are formed by pentamers resulting of the self-assembly of a different protein (in orange). Pores allowing trafficking of molecules are located at the center of each hexamer and pentamer. Sizes can range from 20-25 nm for the encapsulin shell to 100-150 nm for carboxysomes.

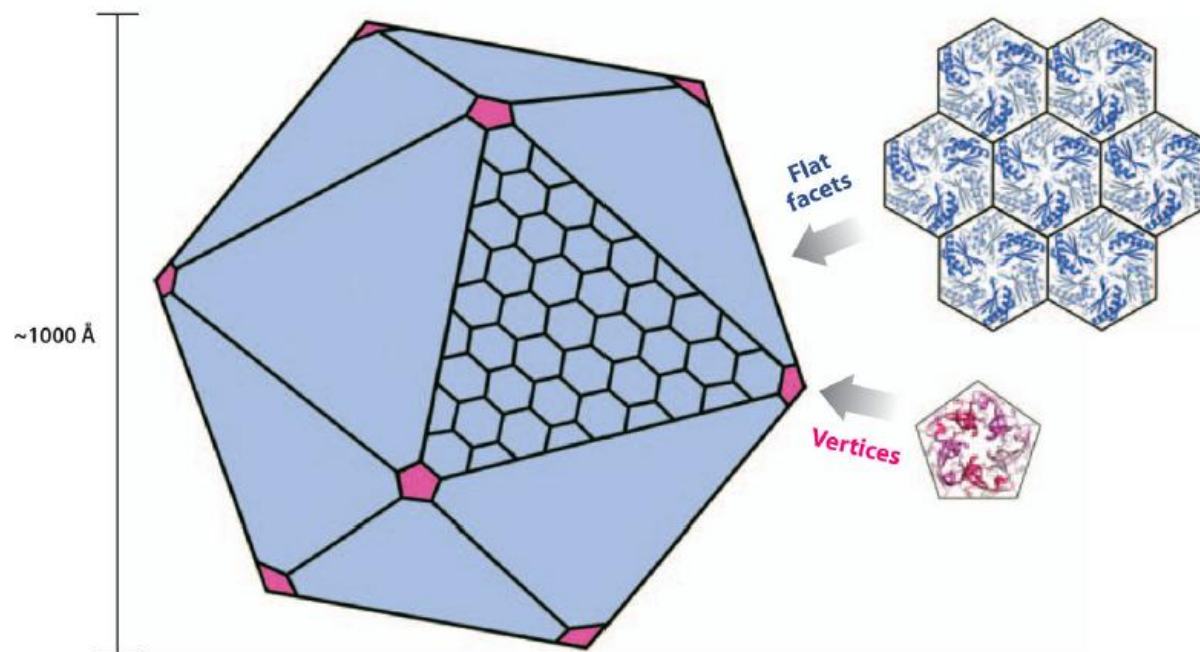
a



b



c



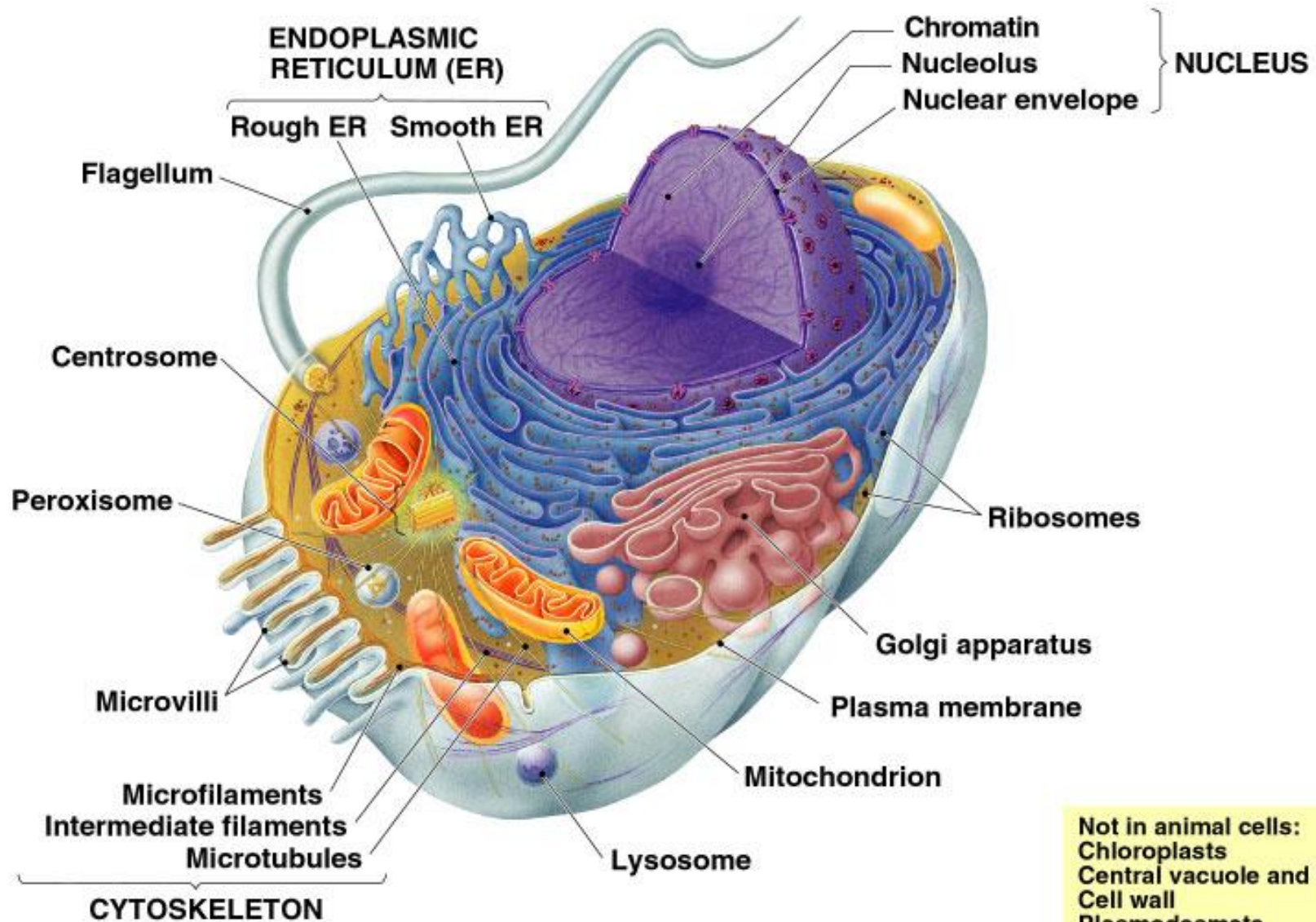
→ see reviews from

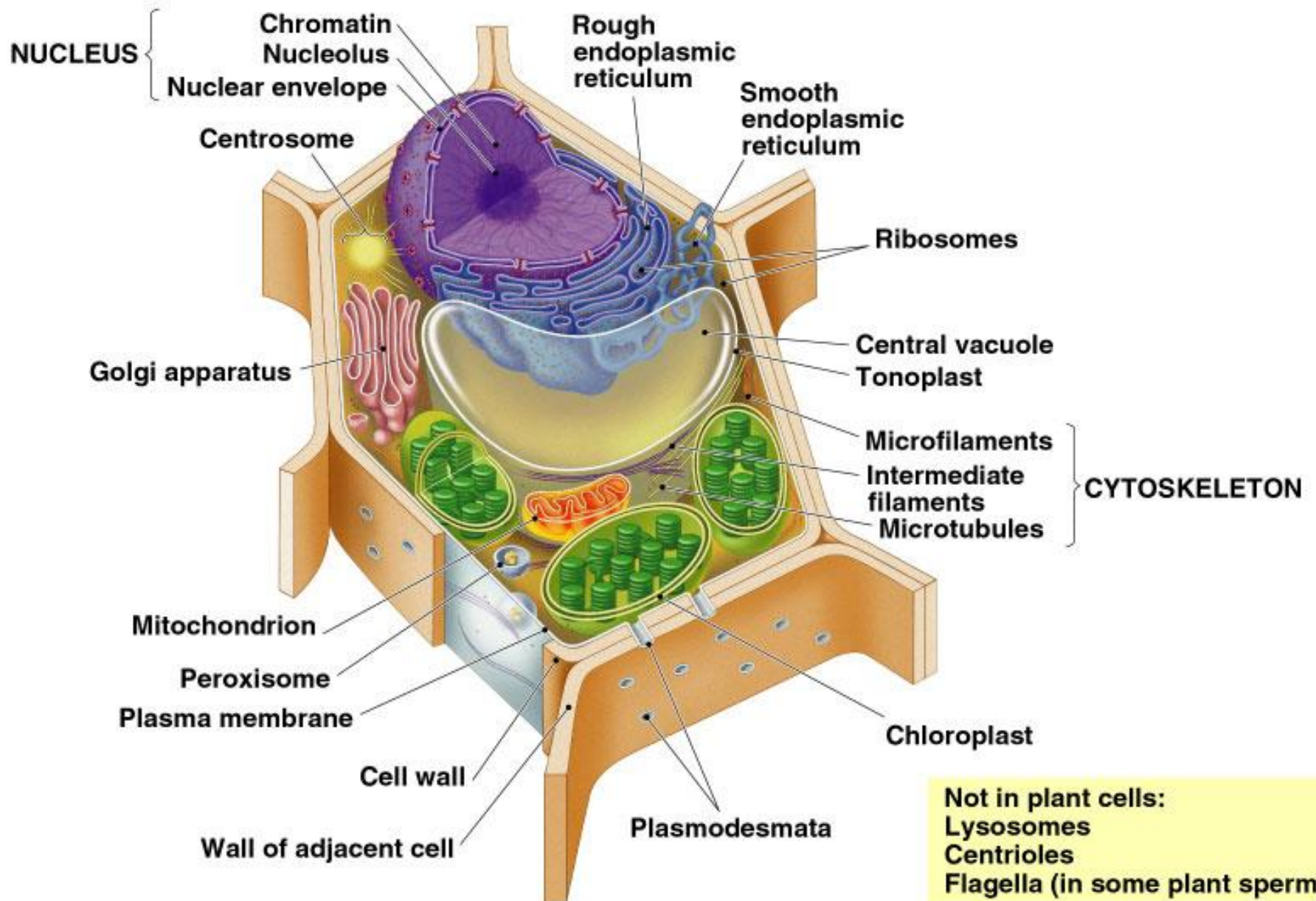
http://cshperspectives.cshlp.org/site/misc/cell_biology_of_bacteria.xhtml

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Eukaryotic compartments and cell structure





Animal cells, yeast cells

Plant cells

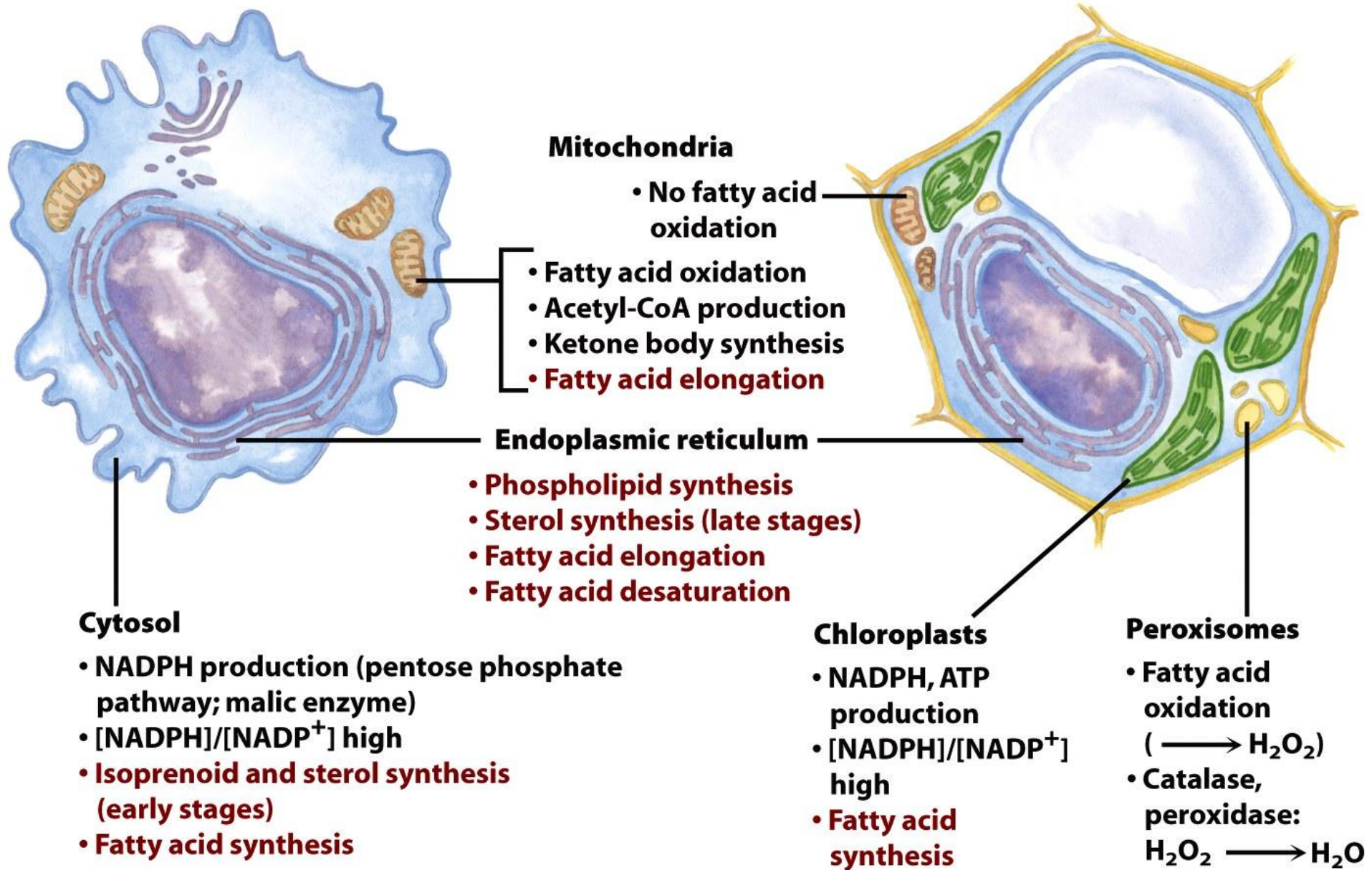


Figure 21-8
Lehninger Principles of Biochemistry, Fifth Edition
 © 2008 W. H. Freeman and Company

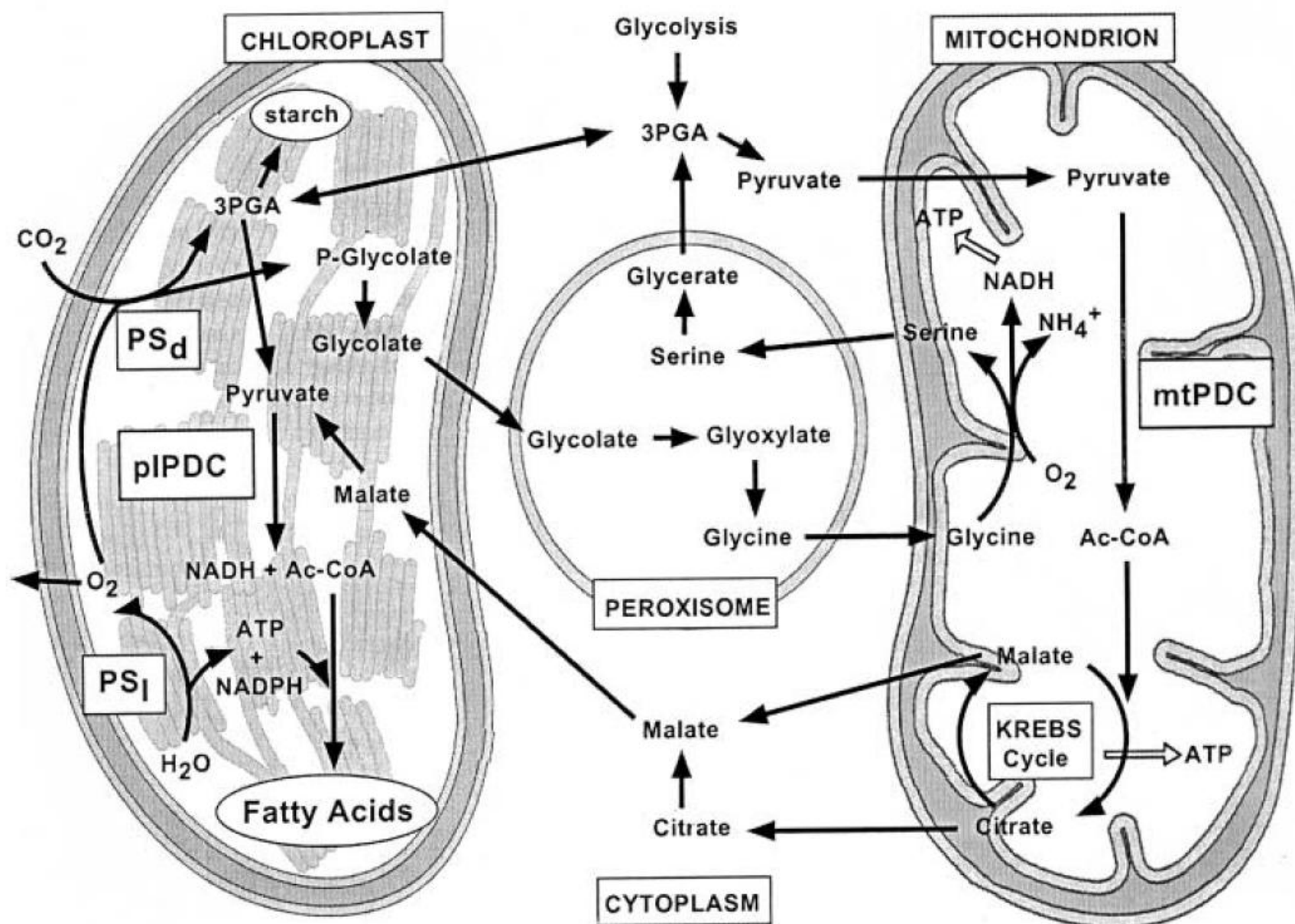
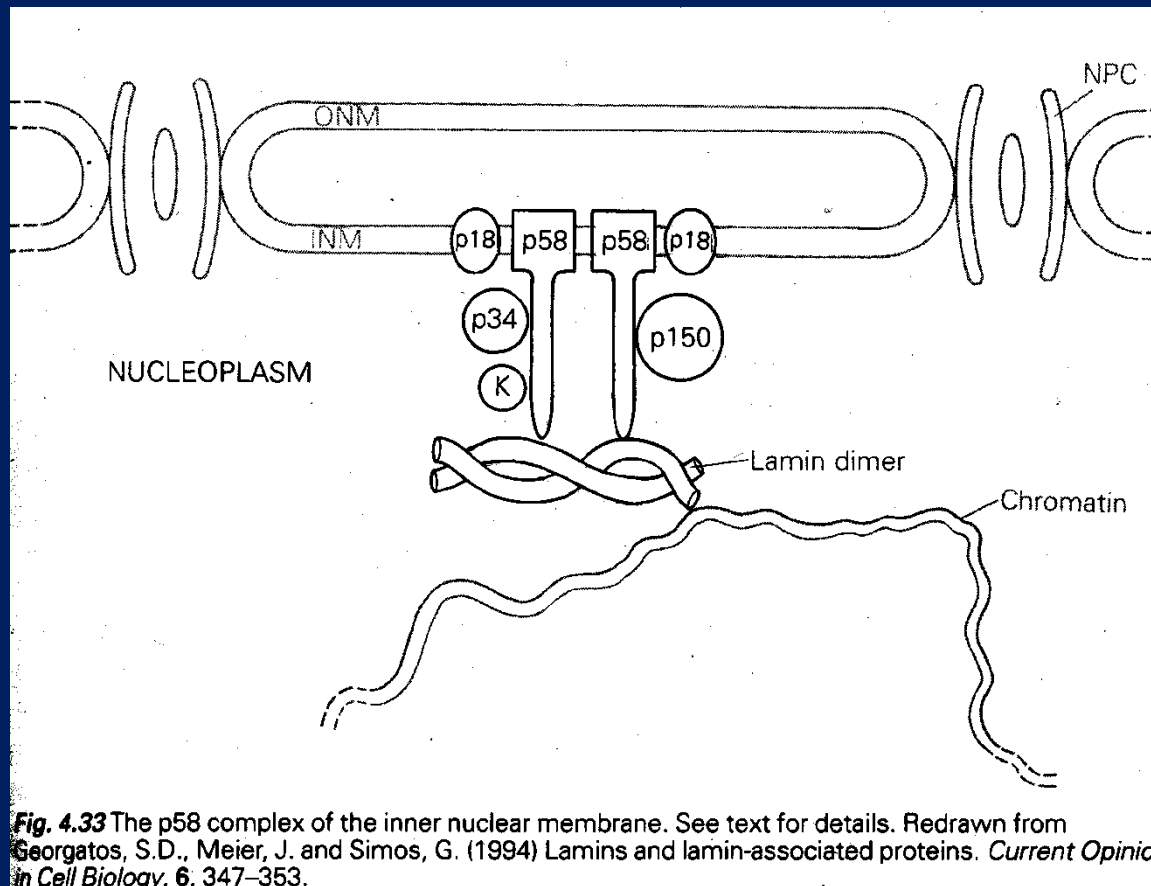
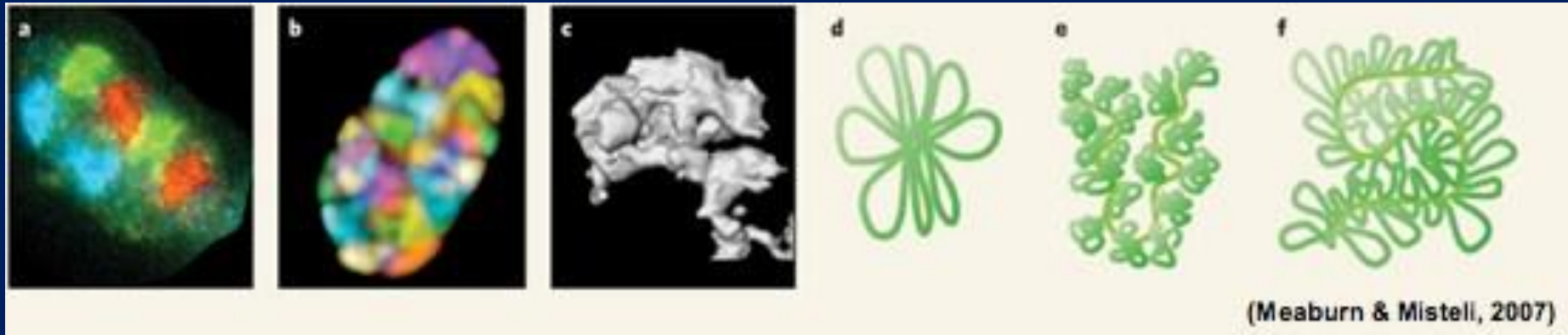


Fig. 1. Compartmentalization of metabolism in plant cells. PS_I, the light reactions of photosynthesis; PS_d, the dark reactions of photosynthesis.

Участие белков в организации хроматина в ядре



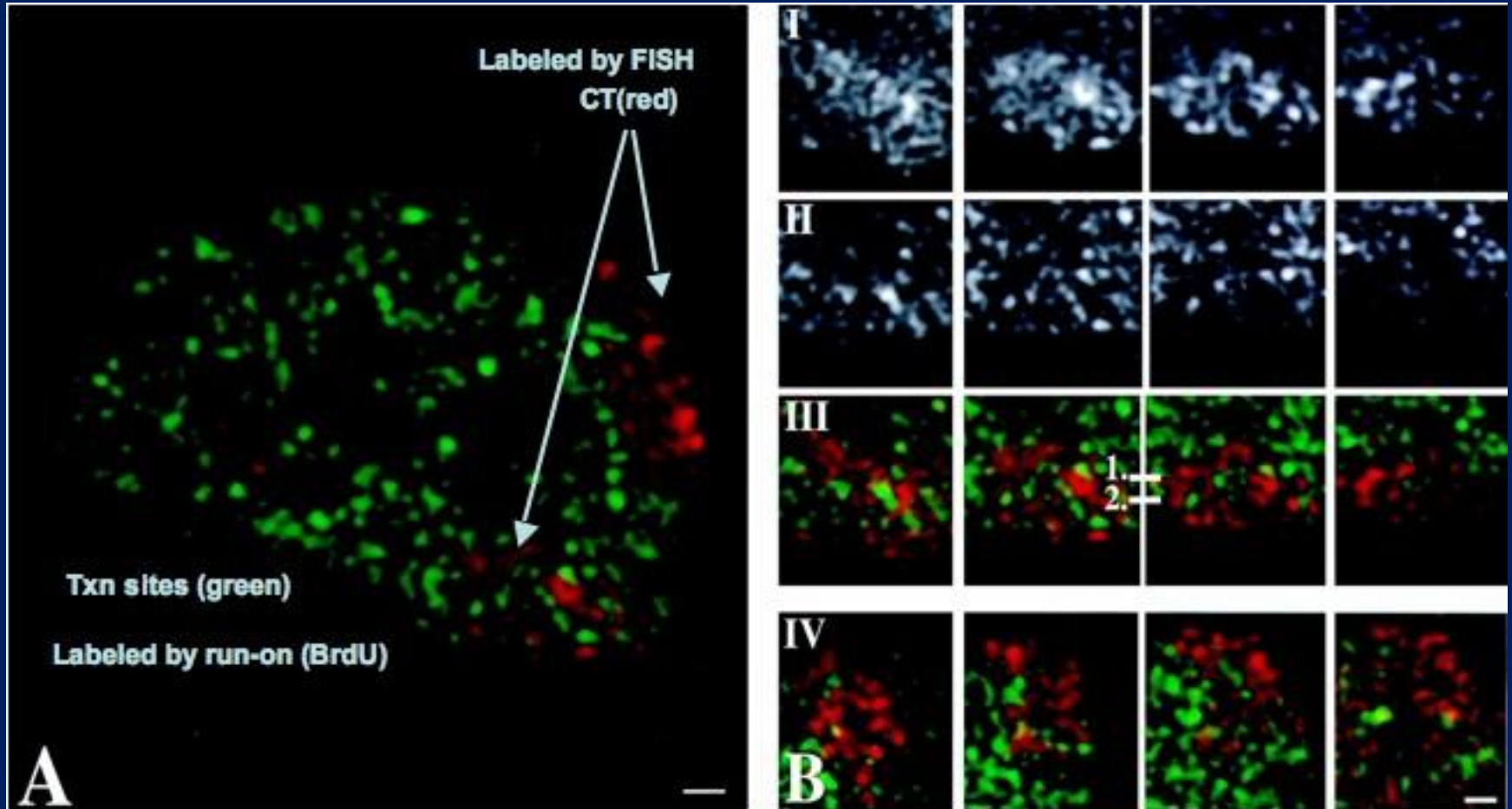
Chromosome Territories



- Individual chromosomes are organized into chromosome territories (CTs)
- Chromatins are dynamic - interactions with nuclear architecture
- Correlation between CT structure and function (active vs. inactive X chromosome)

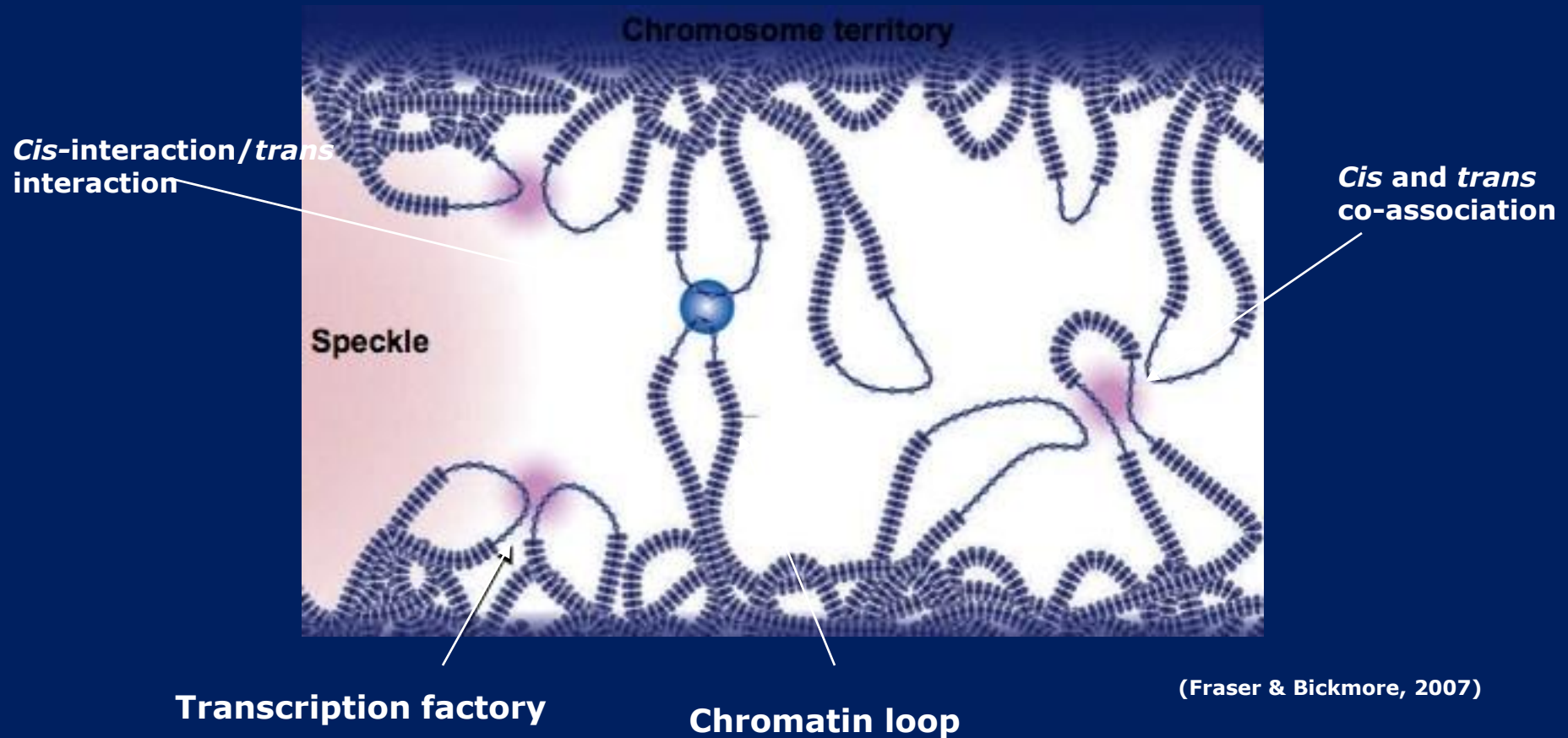
Purpose: to facilitate/regulate gene expression

Correlation between chromosome territories & gene activity

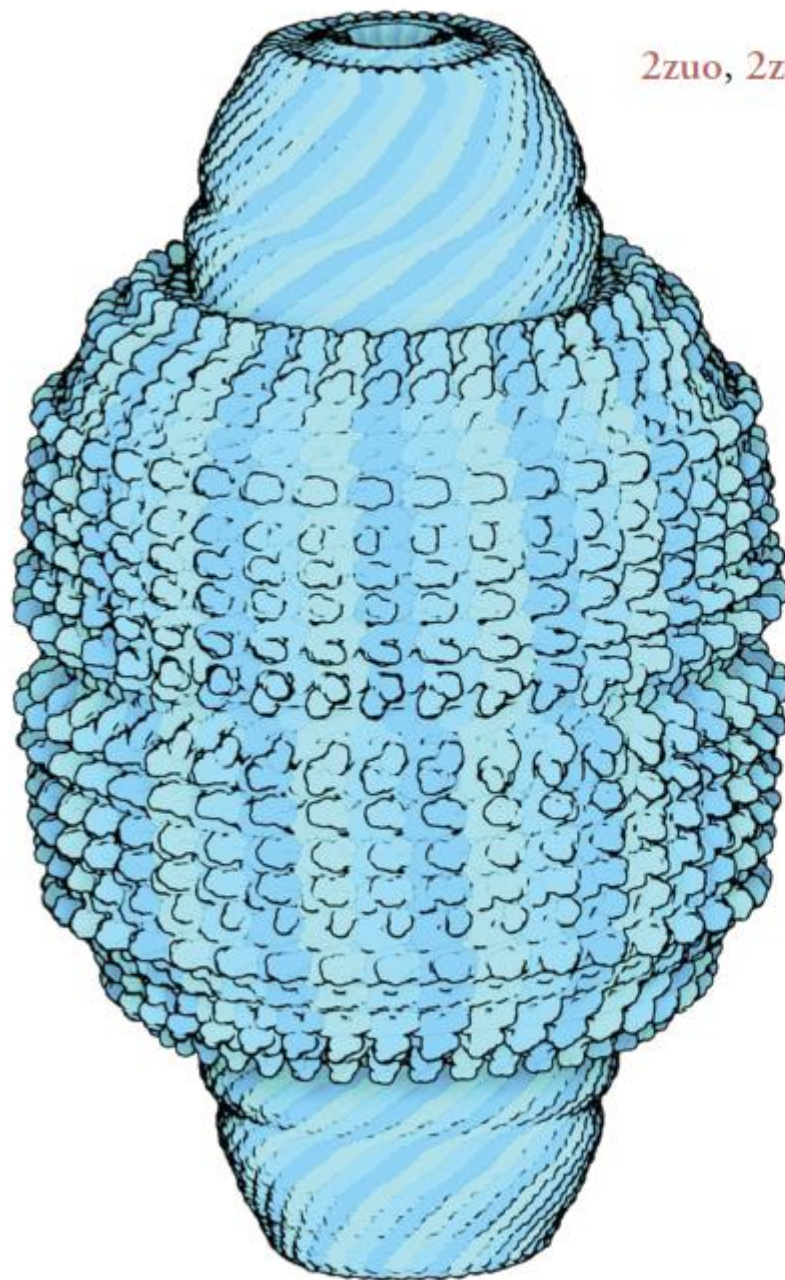


Distribution of transcription sites in relations to CTs

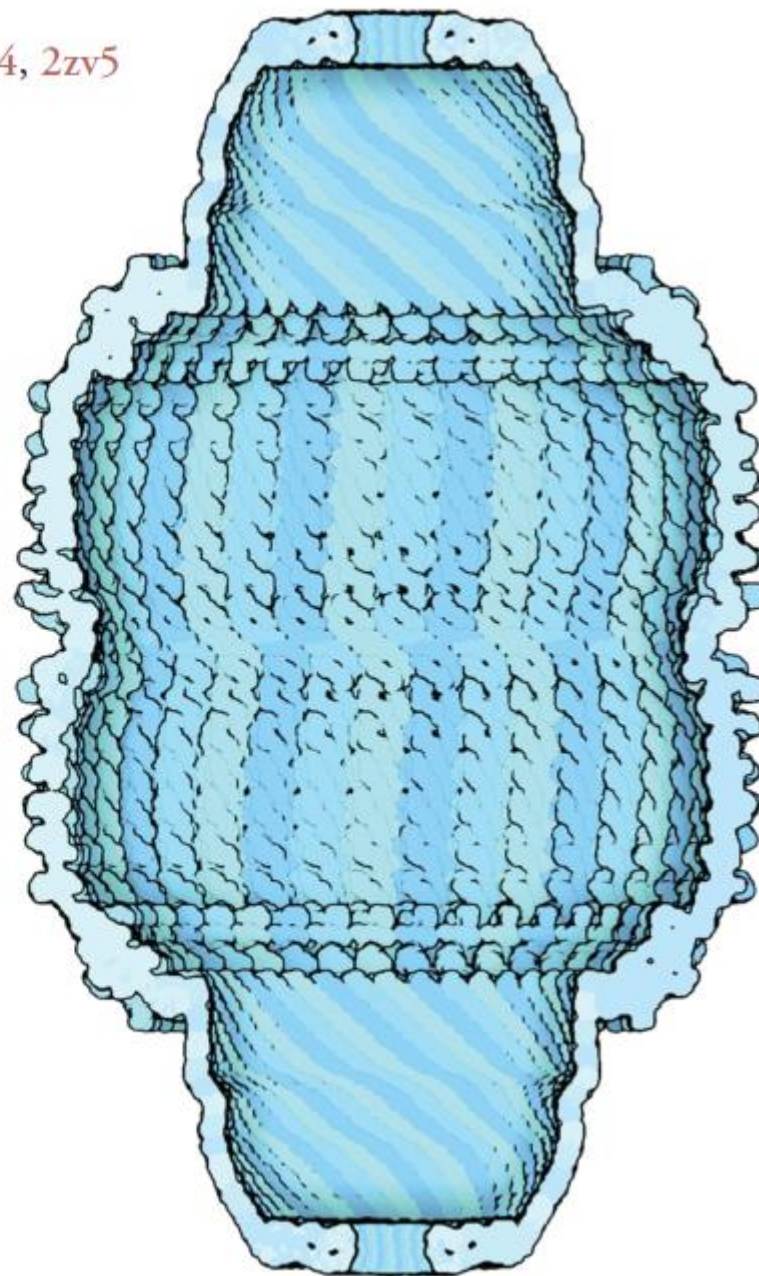
Colocalization of genes in the nucleus for expression or coregulation



Correlation between chromosome location and gene expression



2zu0, 2zv4, 2zv5



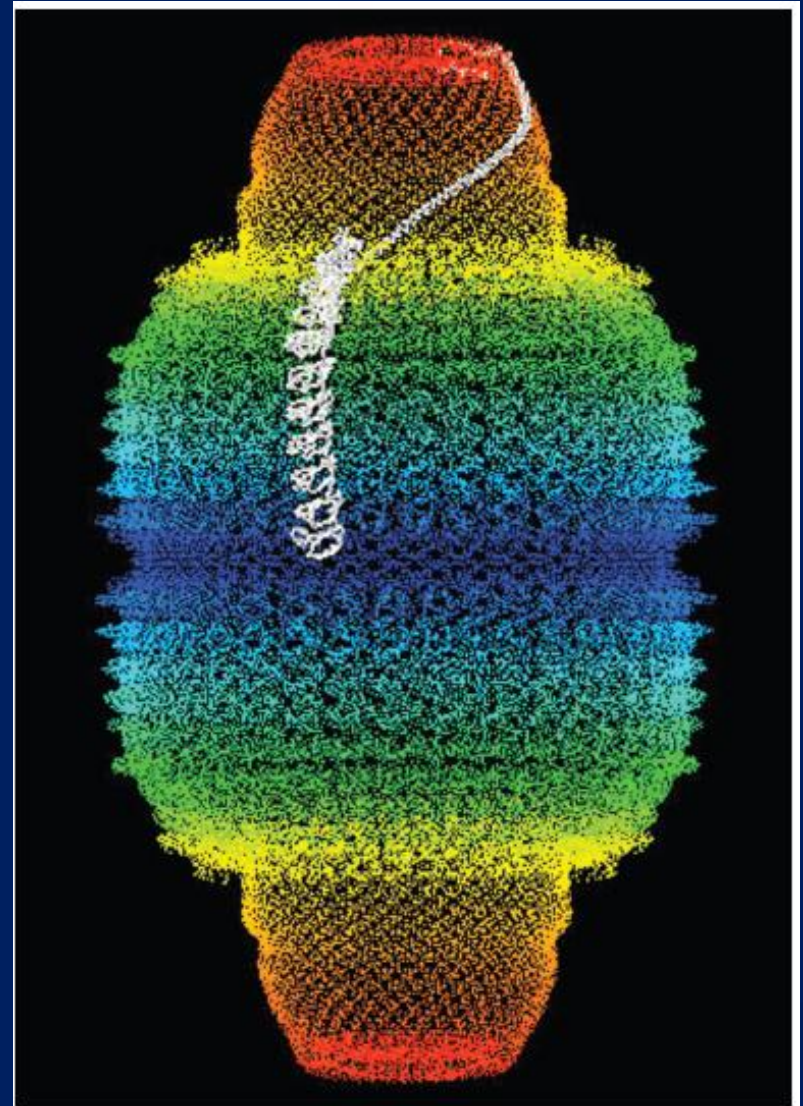
Vaults are composed of many copies of the major vault protein, which assembles to form a hollow football-shaped shell. Inside cells, the vault also encloses a few other molecules, which were not seen in the crystal structure because they don't have a symmetrical structure inside the vault. **These molecules include several small RNA molecules, a protein that binds to RNA, and an enzyme that adds nucleotides to proteins.**

They are found in many types of cells (each of our own cells contain about 100,000 of them) **but some organisms, such as fruit flies and yeast cells, don't have them at all.** They are often found in the cytoplasm, where they are transported rapidly from site to site. But, they are also found occasionally in the nucleus, and even more interestingly, they have been found in nuclear pores.

These findings, along with lots of other observations, suggest that vaults may be used for transport.

Definitive proof, however, still remains to be discovered.

The vault is a huge symmetrical structure composed of 78 identical chains. In this picture, one of the chains is colored white and the others are colored from red to blue from one end of the chain to the other. Part of the protein folds into a string of small domains that together assemble into the wide body at the center. The rest of the protein forms a long alpha helix that assembles into the narrow cap at the ends. The vault is so large that the coordinates have been split into three PDB entries ([2zuo](#), [2zv4](#), and [2zv5](#)) so watch your step when you go to explore this structure yourself!



Interactions between antitumor drugs and vault RNA

Tsukasa Mashima¹, Michiko Kudo², Yusuke Takada¹, Akimasa Matsugami¹, Subash C. B. Gopinath³, Penmetcha K. R. Kumar³ and Masato Katahira^{1,4}

Vaults are barrel-shaped particles with a mass of 13 MDa, the largest ribonucleoprotein complex of eukaryotic cell. It is supposed that vaults may play an important role in intracellular detoxification processes, and thus function in the multidrug resistance (MDR) of cancer cells (1, 2). It is suggested that the entire vault particle is up-regulated in MDR and that a threshold level of vaults is required to impart MDR (3). The human vault constitutes of three proteins and three non-coding RNAs (hvg-1, hvg-2 and hvg-3). Until very recently, however, no vault components that directly interact with the chemotherapeutic compound have been identified, and thus the function of vaults has remained unclear.

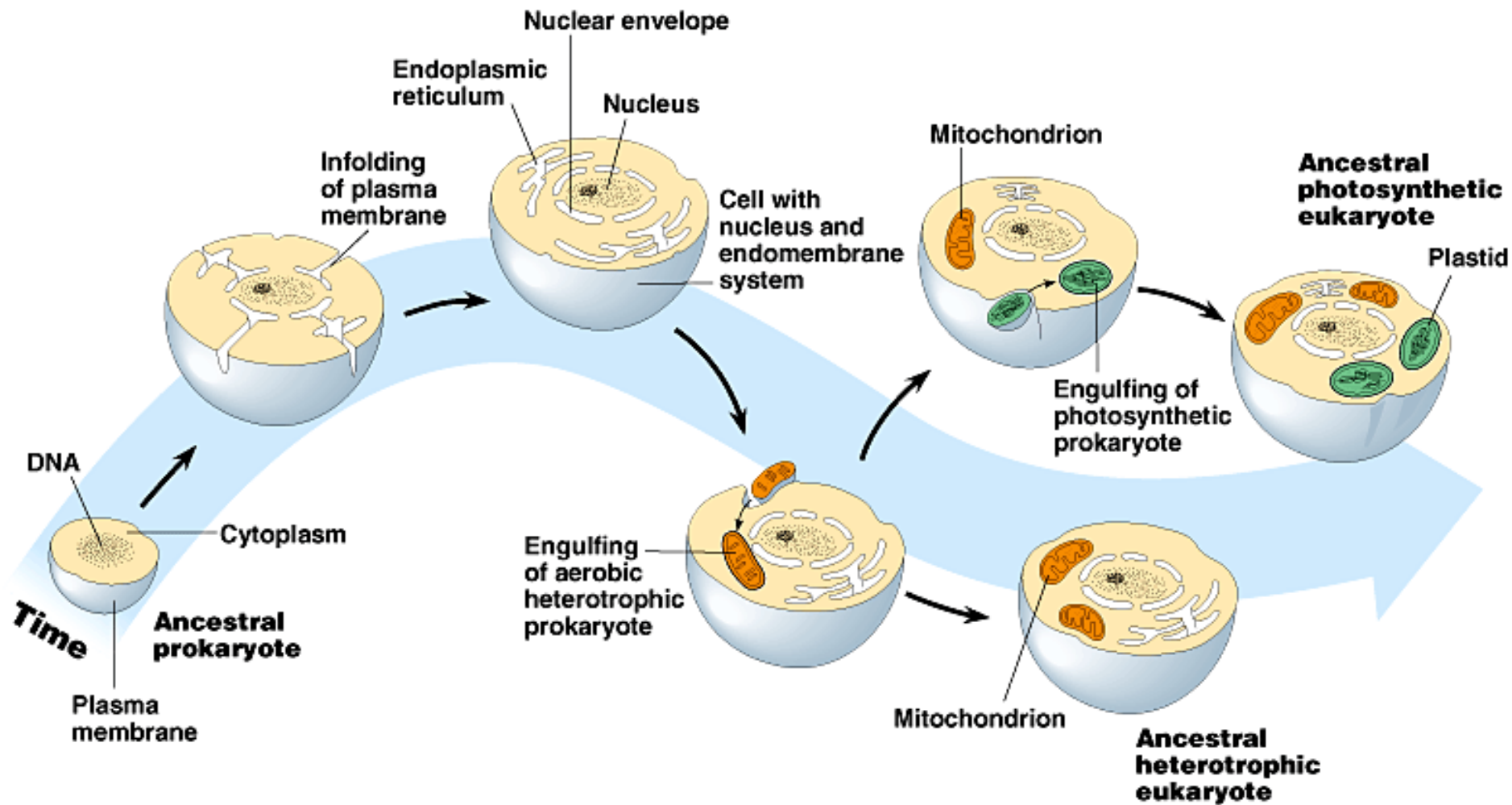
We showed that RNA components of the vault (vRNA), specifically the hvg-1 and hvg-2, bind to a chemotherapeutic compound, mitoxantrone (4). The mitoxantrone binding region within vRNAs was identified with an in-line probing assay (4). The interactions between vRNAs and mitoxantrone under the cellular conditions were also detected. Thus, vRNAs have the ability to bind certain chemotherapeutic compounds. The interactions may be critical for the export of toxic compounds.

Origin and early diversification of eukaryotes

Endomembranes contributed to larger, more complex cells

Endomembranes evolved from in-foldings of prokaryotic membranes.

Endomembranes allowed for compartmentalization of cellular functions. This contributed to the evolution of increasing complexity and development of new functions.



Mitochondria and chloroplasts (and maybe other organelles) evolved from endosymbiotic bacteria.

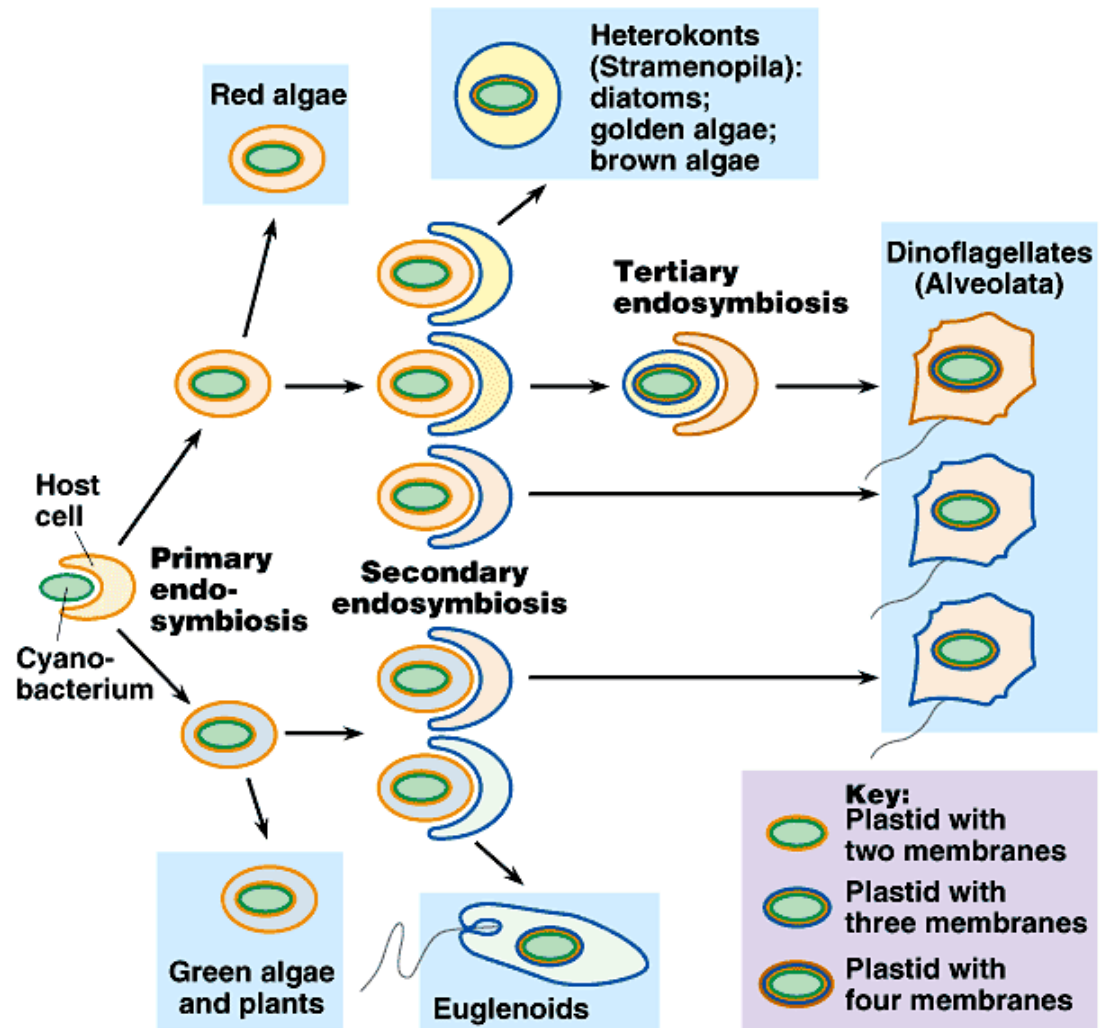
Heterotrophic prokaryotes were engulfed and function as mitochondria.

Photosynthetic prokaryotes were engulfed and function as chloroplasts.

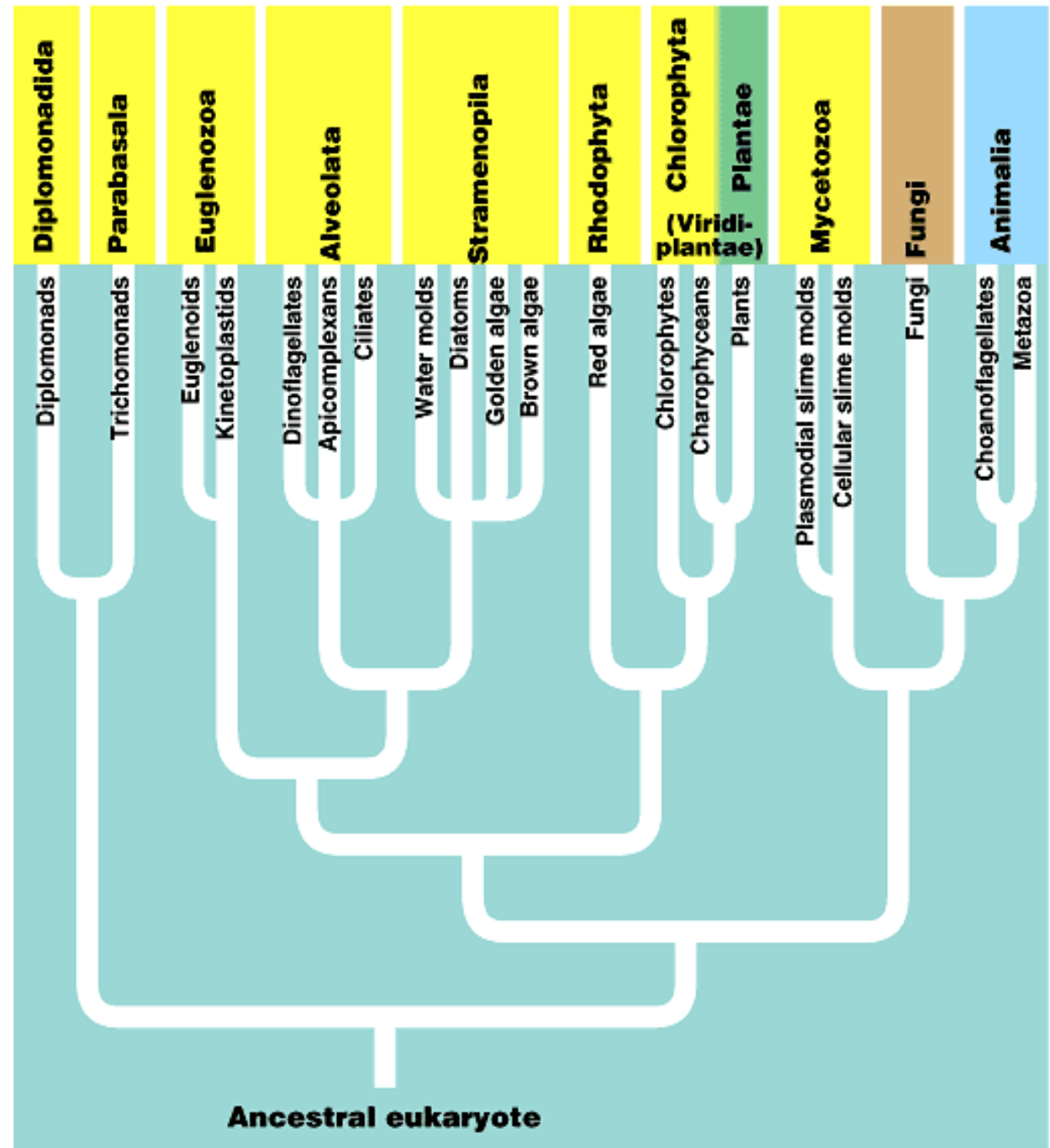
Eukaryotic cell is a chimera of prokaryotic ancestors [The term chimera refers to the mixture of three prokaryotes].

- a. Original contributes genome**
- b. One becomes mitochondrion**
- c. One becomes chloroplast**

- ◆ Photosynthetic protists have evolved in several clades that also have heterotrophic members.
- ◆ Different episodes of secondary endosymbiosis account for the diversity of protists with plastids.



A “wave” of diversity followed the origin of eukaryotes.

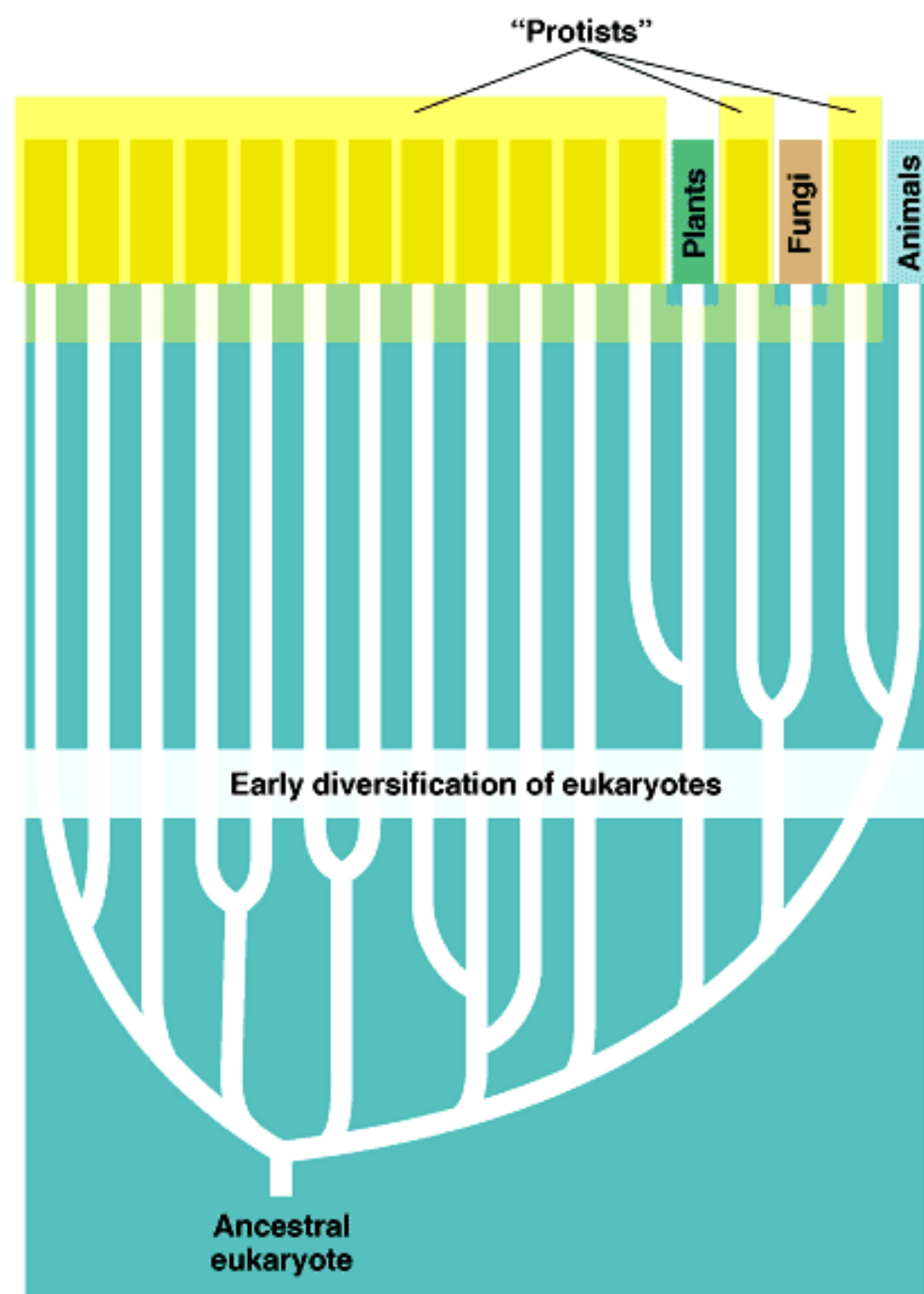


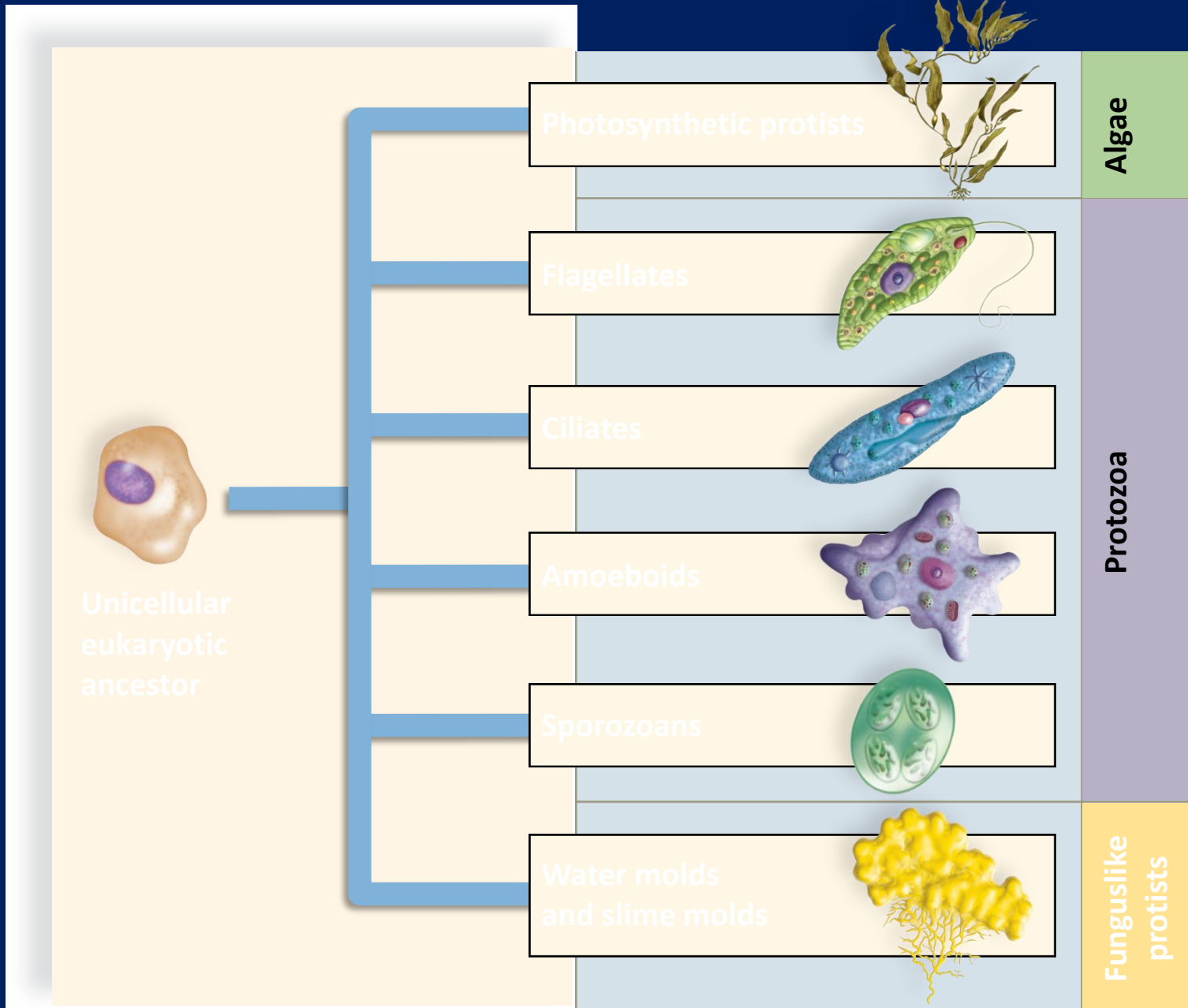
Introduction to the protists

Systematists split protists into many kingdoms

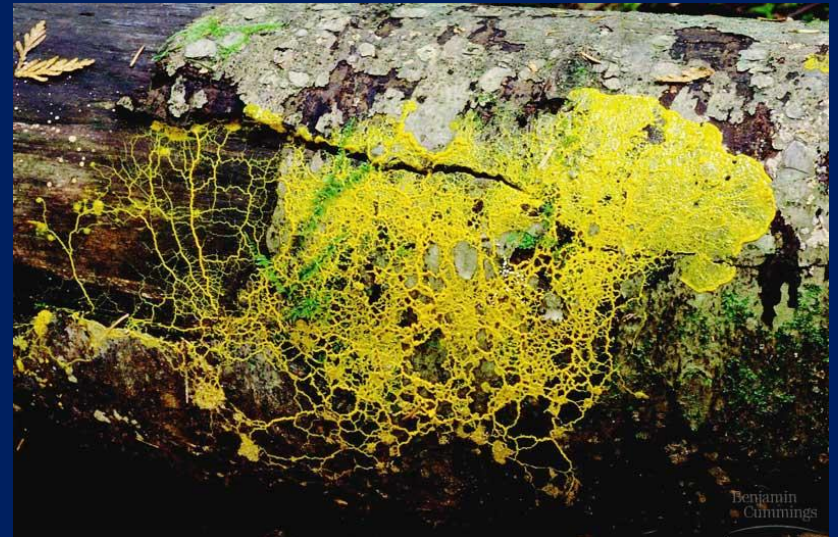
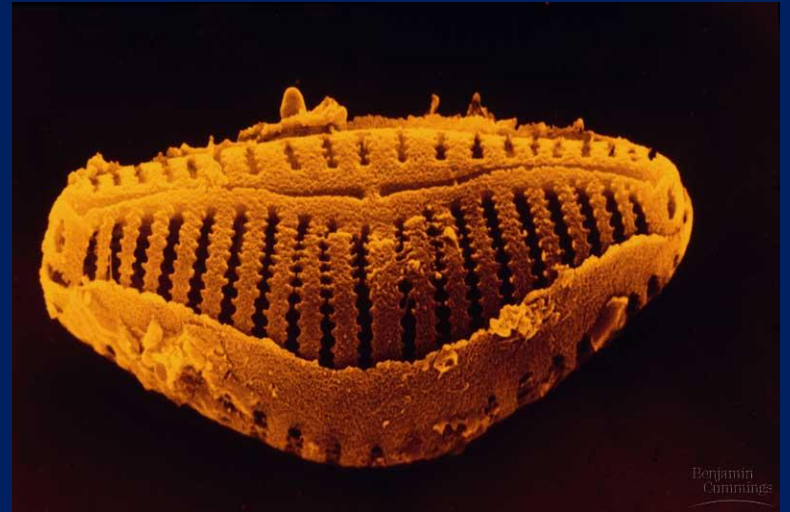
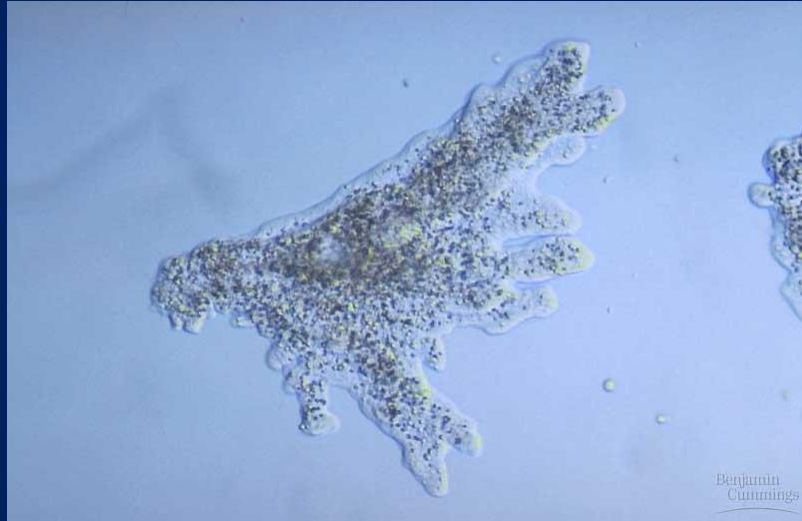
In the five kingdom system, anything that wasn't a prokaryote, plant, animal, or fungus was grouped as a protist.

Systematists now divide protists into as many as 20 separate kingdoms.





Protists are the most diverse of all eukaryotes.



- ◆ All three domains seem to have genomes that are chimeric mixes of DNA that was transferred across the boundaries of the domains.
- ◆ This has lead some researchers to suggest replacing the classical tree with a web-like phylogeny

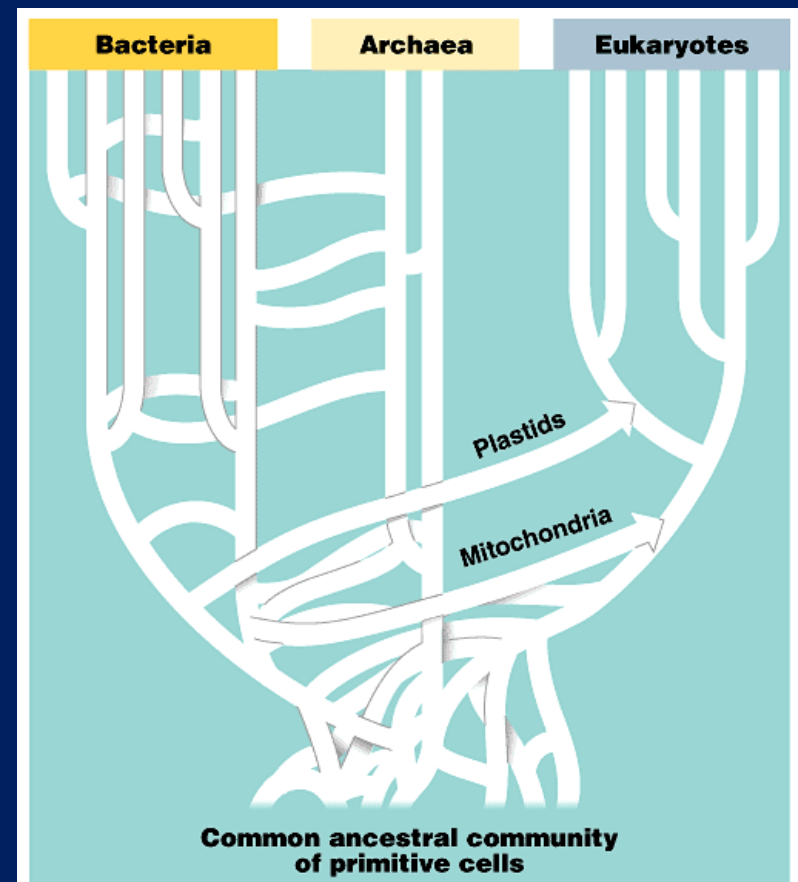
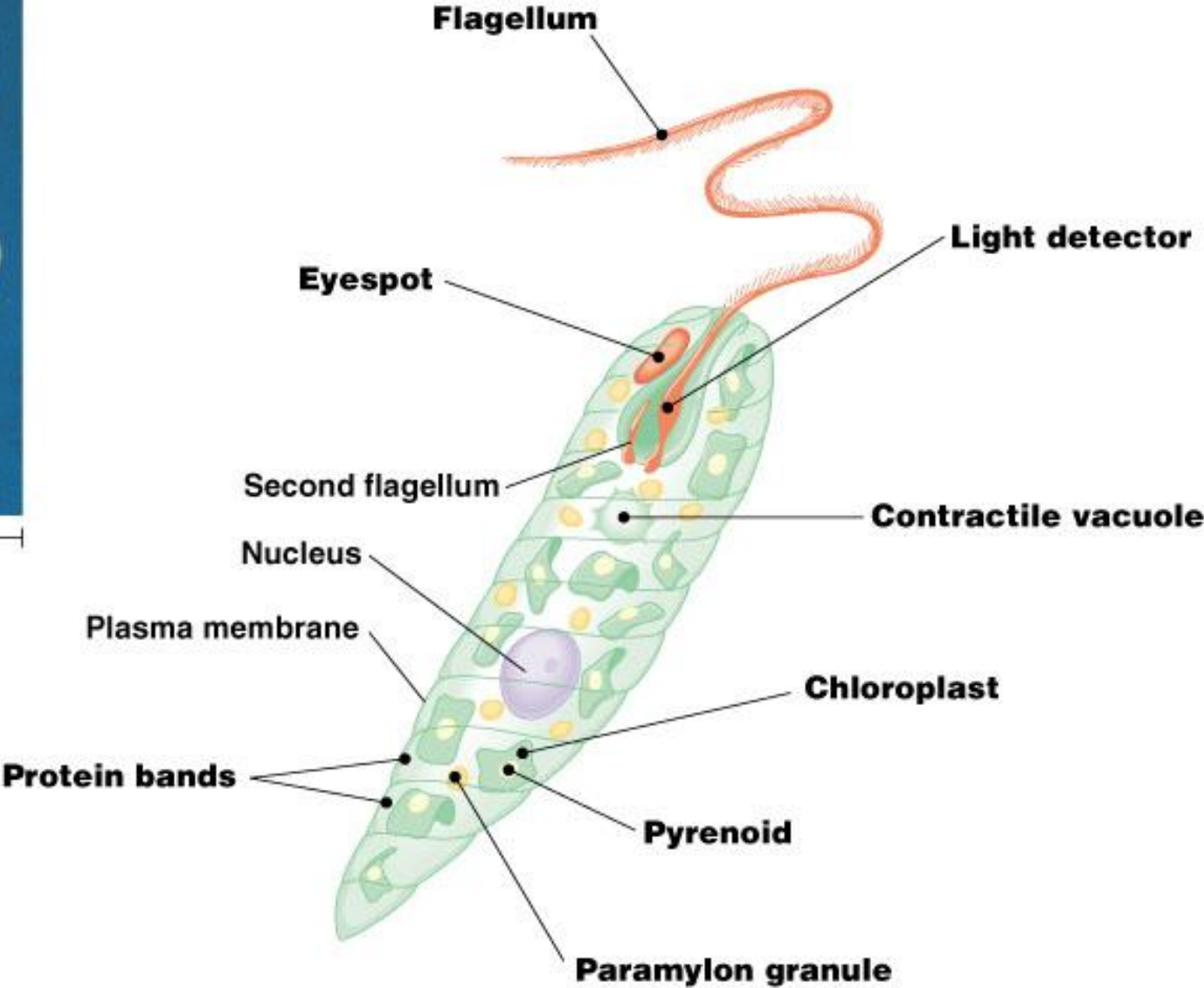


Fig. 28.7



Euglena (LM)

0 μm



General Description of Protists

- Very few general characteristics can be cited without many exceptions.
 - Complex eukaryotes
- Most protists are unicellular, but some are colonial or even multicellular.
- Various modes of nutrition, mobility, etc.

Nutrition

Protists may be autotrophic, heterotrophic, or mixotrophic organisms. Mixotrophic organisms combine photosynthesis and food ingestion.

Photosynthetic: algae (plant-like)

Ingestive: protozoa (animal-like)

Absorptive: fungus-like

Motility

Most protists are motile, with either flagella or cilia. Some move by gliding or by extensions.

Note: Eukaryotic and prokaryotic flagella are *not* homologous structures.

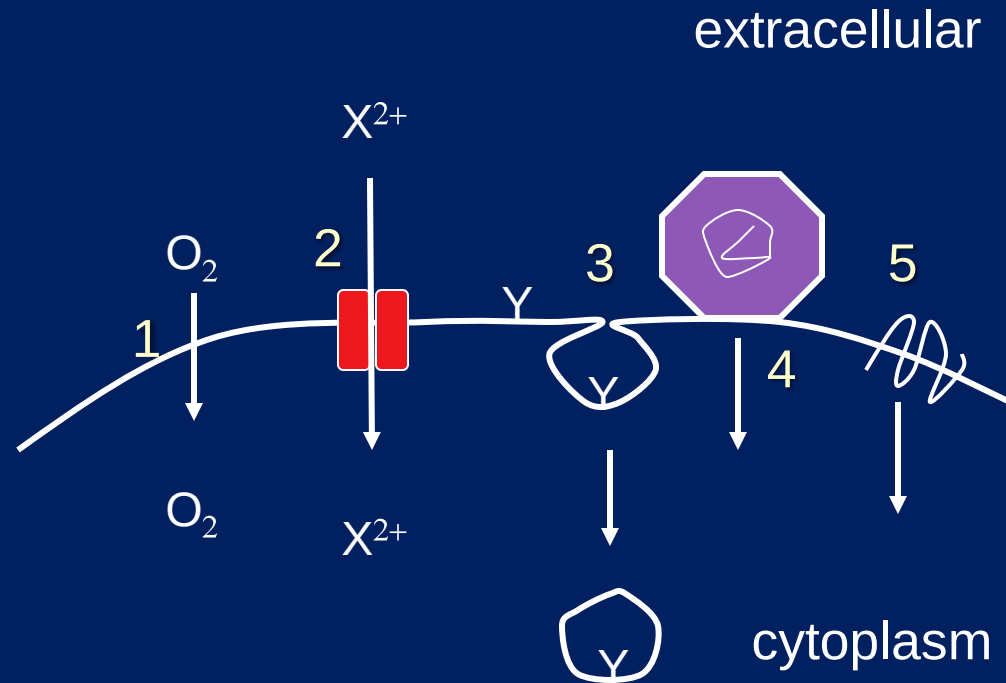
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metabolic reactions are compartmented; biosynthesis and catabolism are usually separated in space;
compartmentation is supported by regulated molecules' transport, sorting and assembly

INTRACELLULAR SORTING OF MOLECULES

Getting molecules into cells: crossing the plasma membrane

1. Diffusion across the plasma membrane / *water, gases, small molecules*
2. Protein-mediated transport / ion channels, transporters
3. Formation and internalization of membrane-limited vesicles/
Endocytosis
Pinocytosis
Phagocytosis
4. Membrane fusion / viruses
5. Pore formation / toxins



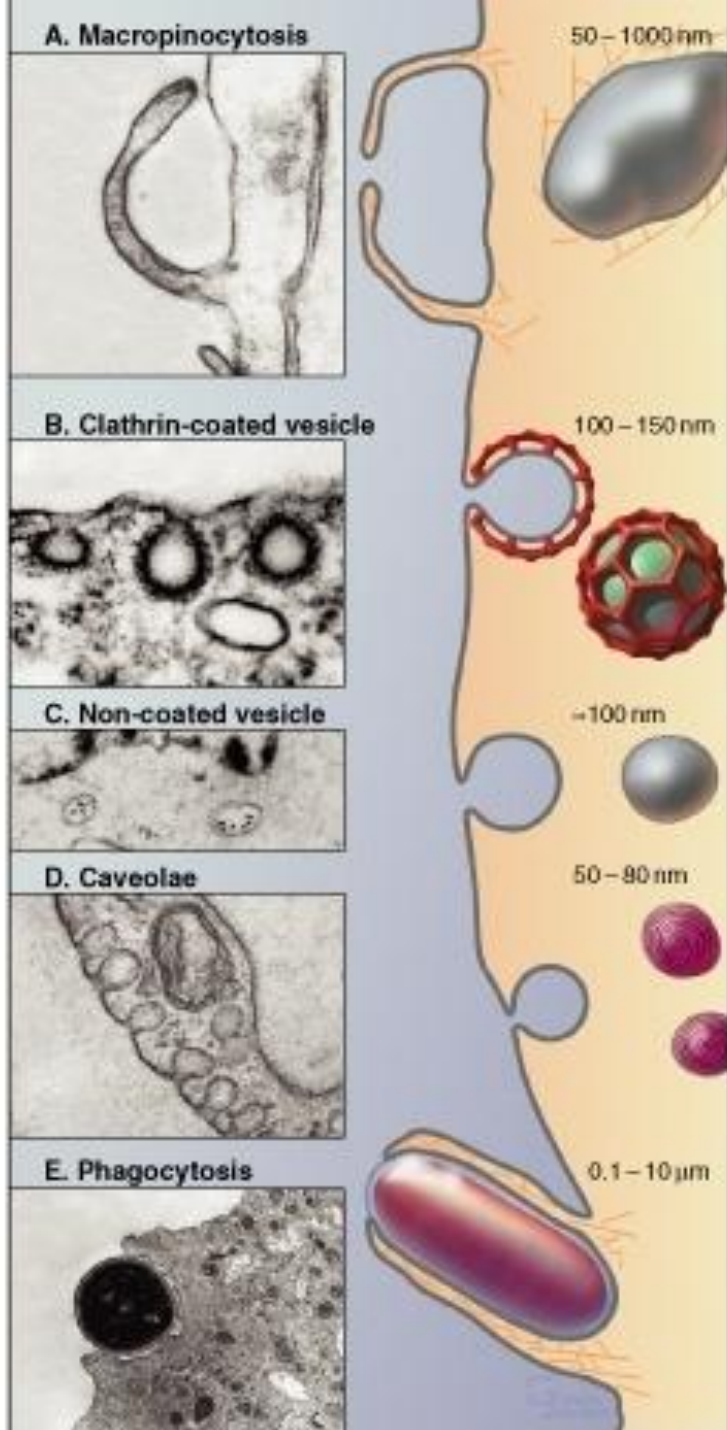
Some of the functions of endocytosis

- ◆ Nutrient uptake
- ◆ Receptor recycling
- ◆ Plasma membrane protein downregulation and/or degradation
- ◆ Synaptic vesicle recycling
- ◆ Transcellular signaling
- ◆ Exploitation: virus and toxin entry into cells

Common features of endocytosis

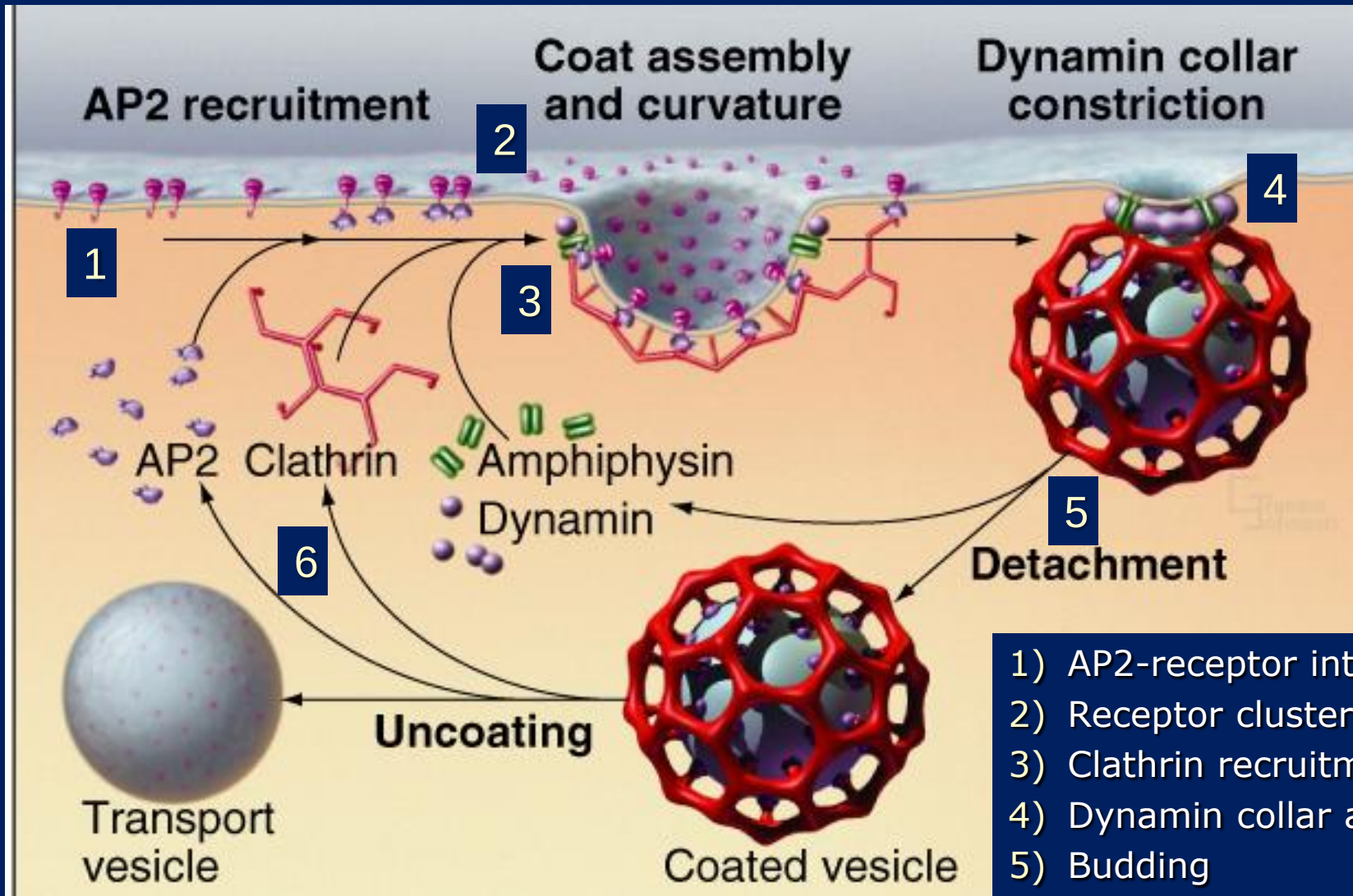
- ◆ Small region of the plasma membrane invaginates to form *membrane-limited vesicles* (0.05-0.1 μ m diameter)
- ◆ Internalized molecules *retain topology* (luminal = extracellular)
- ◆ Cargo can be *specifically selected*
- ◆ Destination of cargo can be *controlled*; destination depends on pathway of uptake
- ◆ *Cargo receptors can be recycled* to the cell surface
- ◆ Conditions under which internalization occurs can be regulated
- ◆ Cytoskeletal and coating proteins involvement

Endocytic Mechanisms



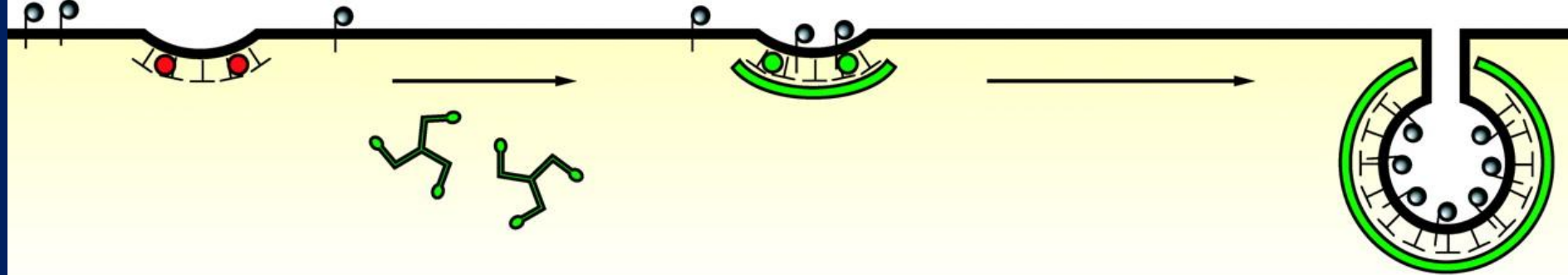
- ◆ clathrin coated pits
- ◆ caveolin coated caveolae
- ◆ non-coated pit pinocytosis
- ◆ cytoskeletal derived
 - macropinocytosis
 - phagocytosis

Formation of Coated Pit



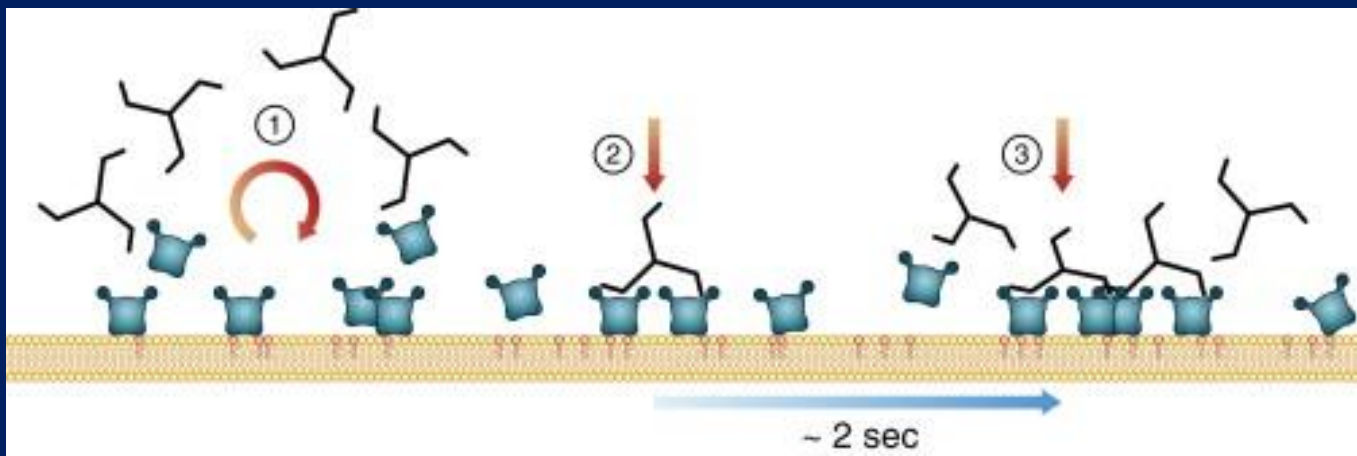
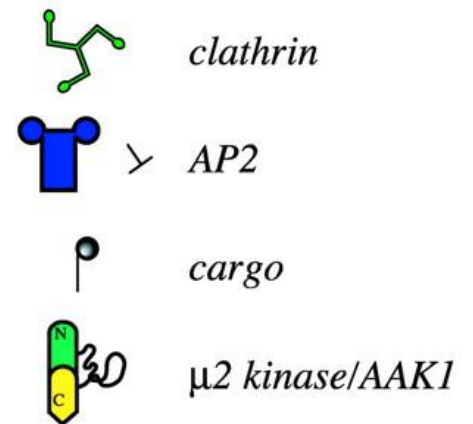
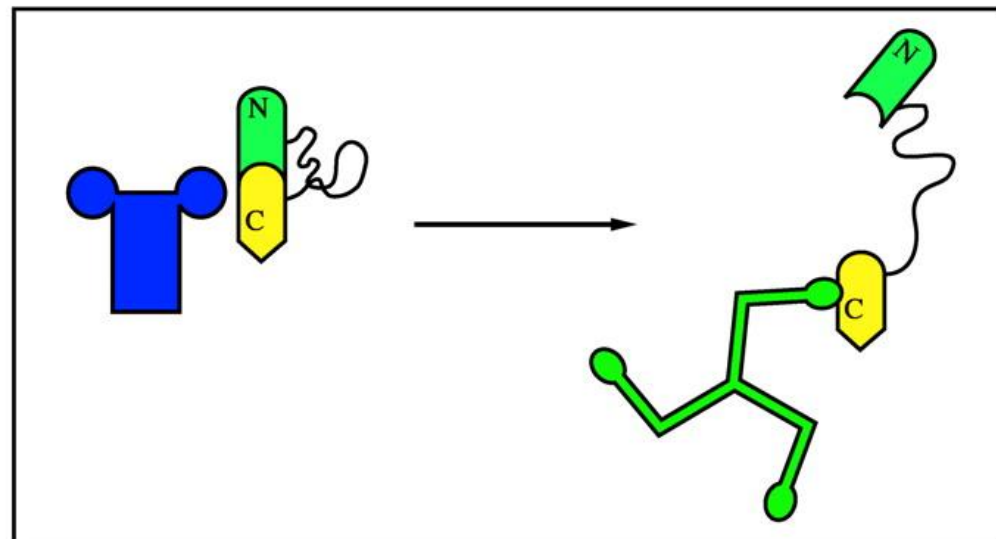
AP=accessory protein

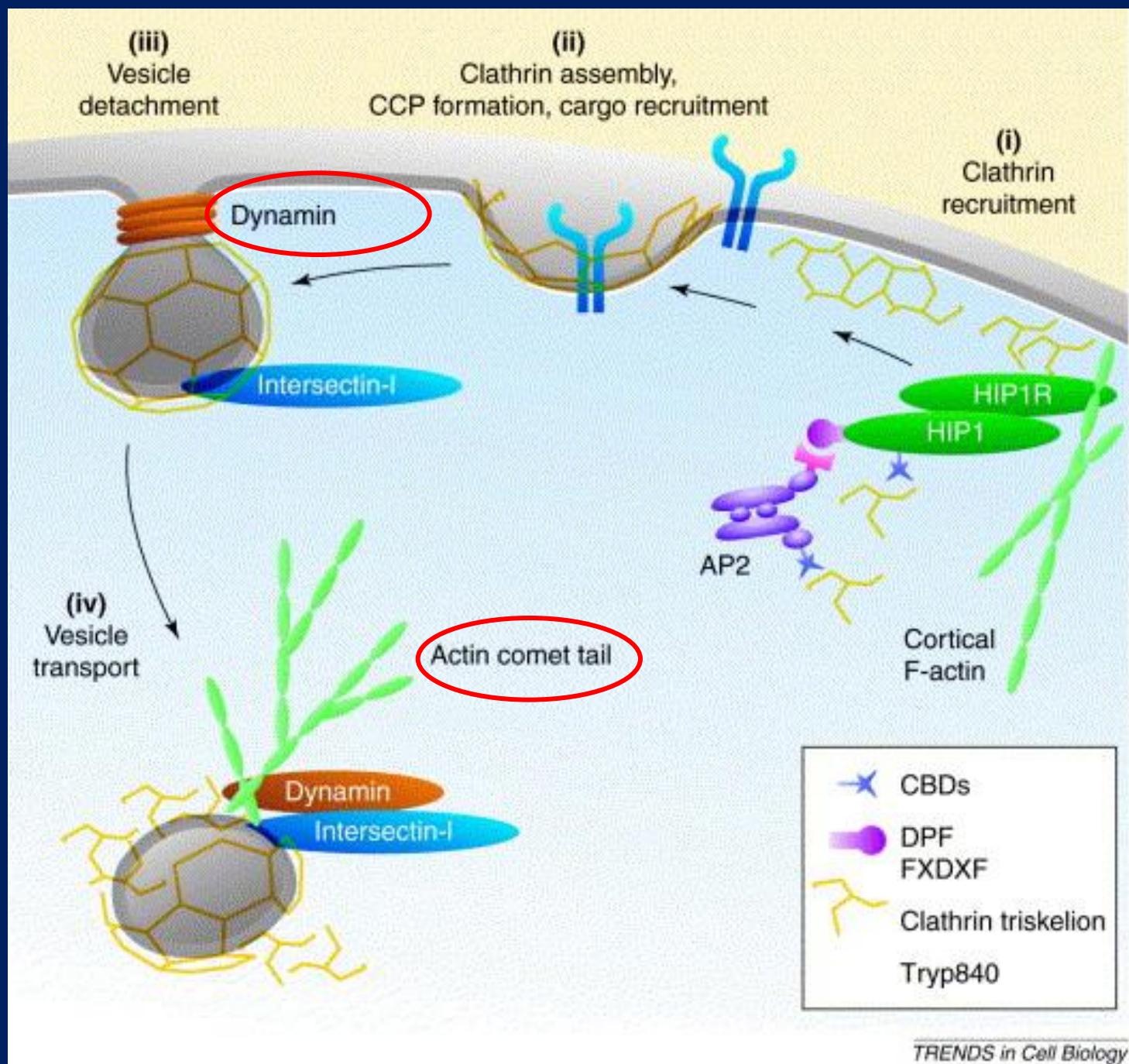
- 1) AP2-receptor interaction
- 2) Receptor clustering
- 3) Clathrin recruitment
- 4) Dynamin collar assembly
- 5) Budding
- 6) Uncoating & recycling of components

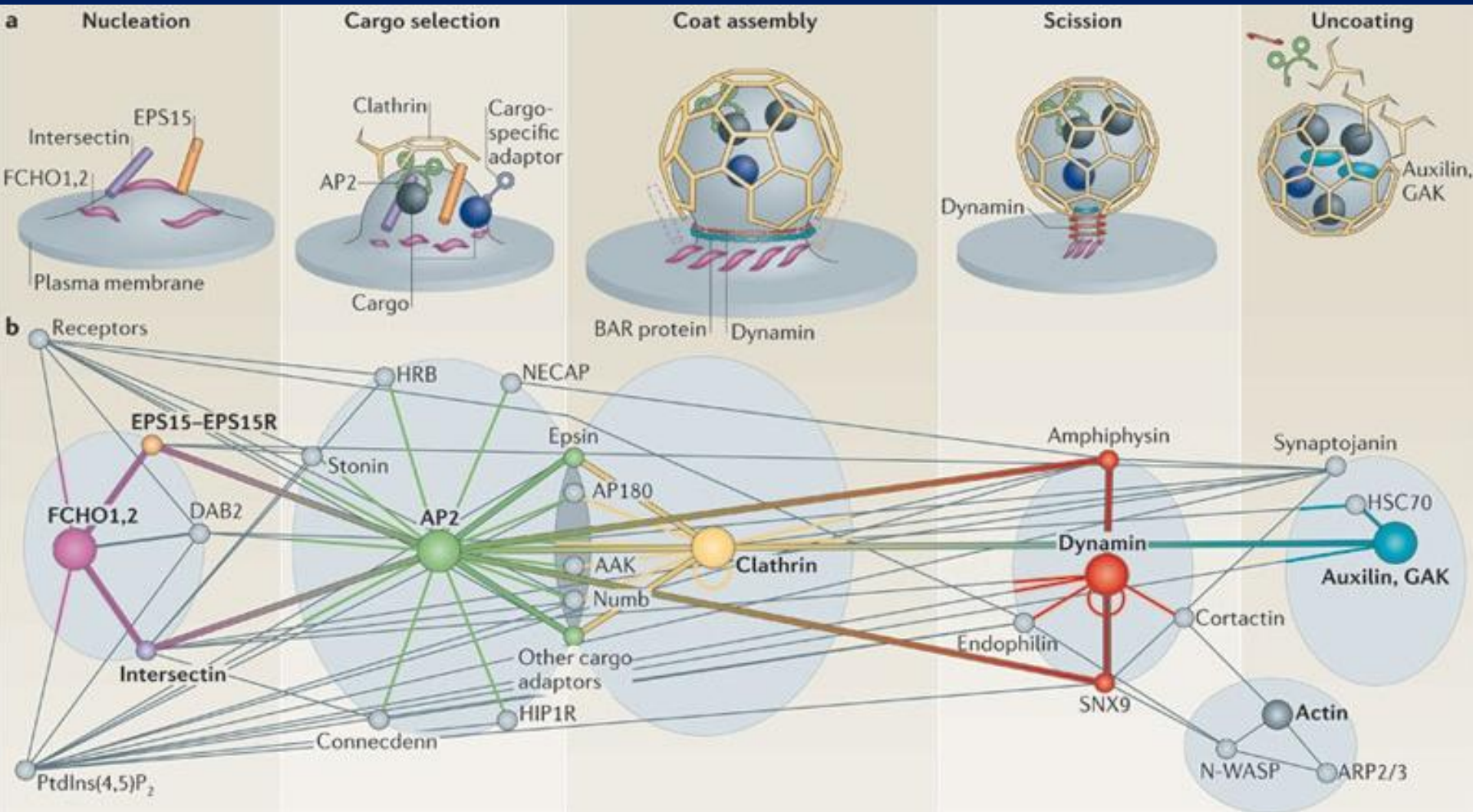


Basal kinase activity ●

Activated kinase ●







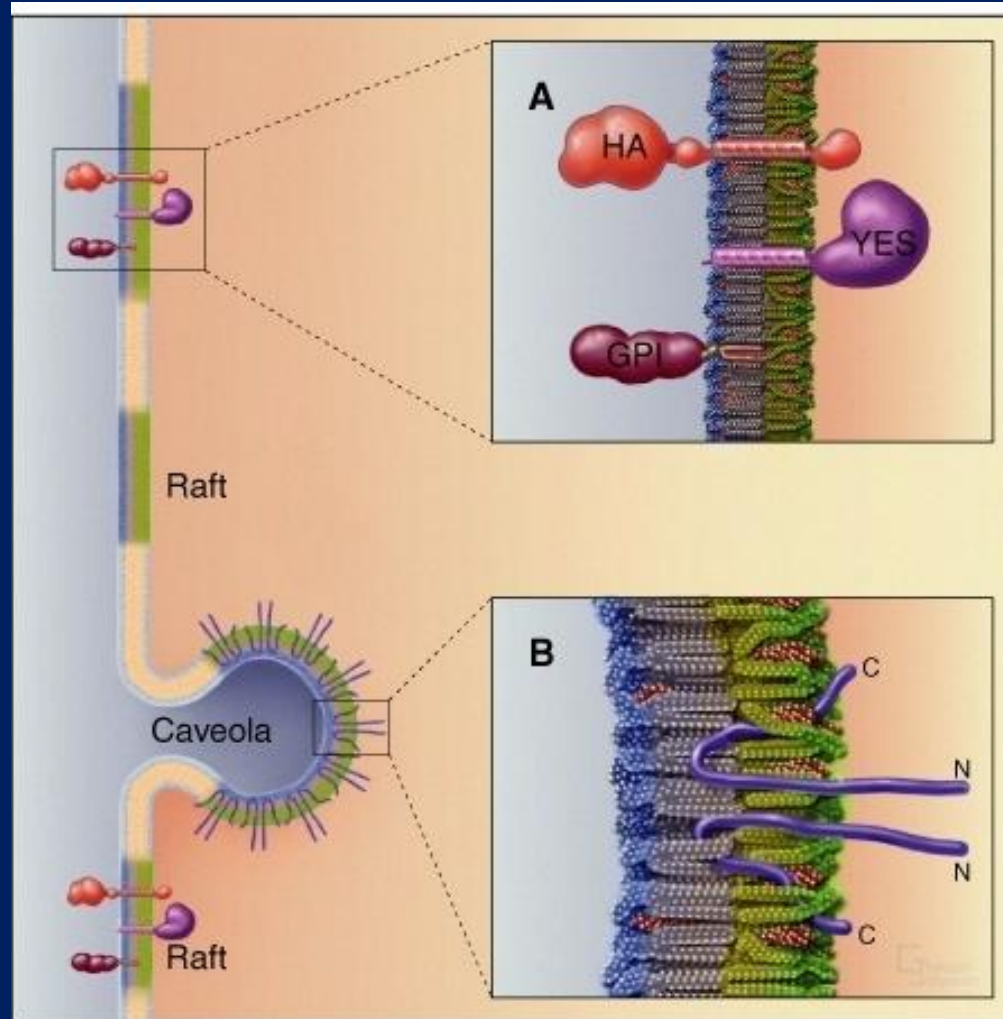
Caveolae



- ◆ Caveolae are 50-100 nm invaginations on the cells surface
 - Caveolin, a membrane protein, is the “coat protein” of caveolae
- ◆ Do not undergo constitutive endocytosis but can undergo **endocytosis in response to a signal** (ex. SV40 binding) in a cholesterol- and dynamin-dependent fashion
- ◆ Internalized caveolae recruit actin to form “comet tails”
- ◆ Upon internalization caveolae are delivered to novel endosomal compartments known as “caveosomes”

Caveolae

- ◆ Associated with lipid rafts
- ◆ Membrane lipid cycling
- ◆ **Raft-associated protein endocytosis/exocytosis**
 - Inner leaflet proteins
 - ◆ acylated proteins
 - ◆ prenylated proteins
 - Outer leaflet proteins
 - ◆ GPI-linked
 - Some TM proteins that interact specifically with glycosphingolipids/cholesterol
- ◆ Caveolin
 - **high-affinity cholesterol binding protein**



Clathrin viz caveolae endocytosis

- ❑ Both caveolae and clathrin-mediated endocytosis involves dynamin
 - ❑ Caveolae endocytosis can be inhibited by dominant negative caveolin
 - ❑ Caveolae endocytosis is inhibited by cholesterol depletion
-
- ◆ Can be Non-clathrin/non-caveolae (Currently poorly understood)

Pinocytosis/ phagocytosis

- ◆ Pinocytosis: internalization of fluid
 - Actin dependent
 - Generated at sites of ruffling at the plasma membrane
 - Includes macropinocytosis (vesicles $> 1 \mu\text{m}$ in diameter) and micropinocytosis (vesicles $< 200\text{nm}$ in diameter)
- ◆ Phagocytosis: internalization of particles
 - Occurs in specialized cells ex. neutrophils and macrophages
 - Actin dependent
 - Clathrin independent
 - Particles $> 0.5 \mu\text{m}$ in diameter

Pretty Colored Vesicles

- ◆ Gold dust through the endolytic pathway
 - coated pits (CP)
 - early endosome (EE)
 - late endosome (LE)
 - lysosome (LY)

